NEW

HOW IT WORKS
BOOK OF

INCREDIBLE SCIENCE

THE FACT-PACKED GUIDE TO THE WORLD AROUND YOU

Digital Edition

FUTURE

FIRST EDITION

INCREDIBLE SCIENCE

It's no secret that humankind has come a long way since Homo sapiens first emerged from among our ape-like ancestors around 130,000 years ago. Yet despite all of our progress to date, many questions remain. What are we exactly? How do our brains really work? How have we achieved so much in the field of science, and where are we heading next?

In this bookazine you'll journey from our early beginnings as a species, exploring how we came to be and how our immune systems, emotions and even fears develop. You'll then meet some of science's greatest minds and discover for yourself how humans have created vaccines, illuminated the light spectrum and explained phenomena from 'vampires' to out-of-body experiences.

Finally, you'll explore the power behind nuclear fusion and the endless possibilities offered by quantum mechanics before stepping into a future where many diseases are a thing of the past and cloning yourself could be more than just the stuff of science fiction. A world of incredible science is just over the page.

FUTURE

INCREDIBLE SCIENCE

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Printed by William Gibbons, 26 Planetary Road,
Willenhall, West Midlands, WV13 3XT

Distributed by Marketforce, 5 Churchill Place, Canary Wharf, London, E14 5HU
www.marketforce.co.uk Tel: 0203 787 9001

How It Works Book of Incredible Science First Edition

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Future plc is a public
company quoted on the
London Stock Exchange
(symbol: FUTR)
www.futureplc.com

Chief executive **Zillah Byng-Thorne**
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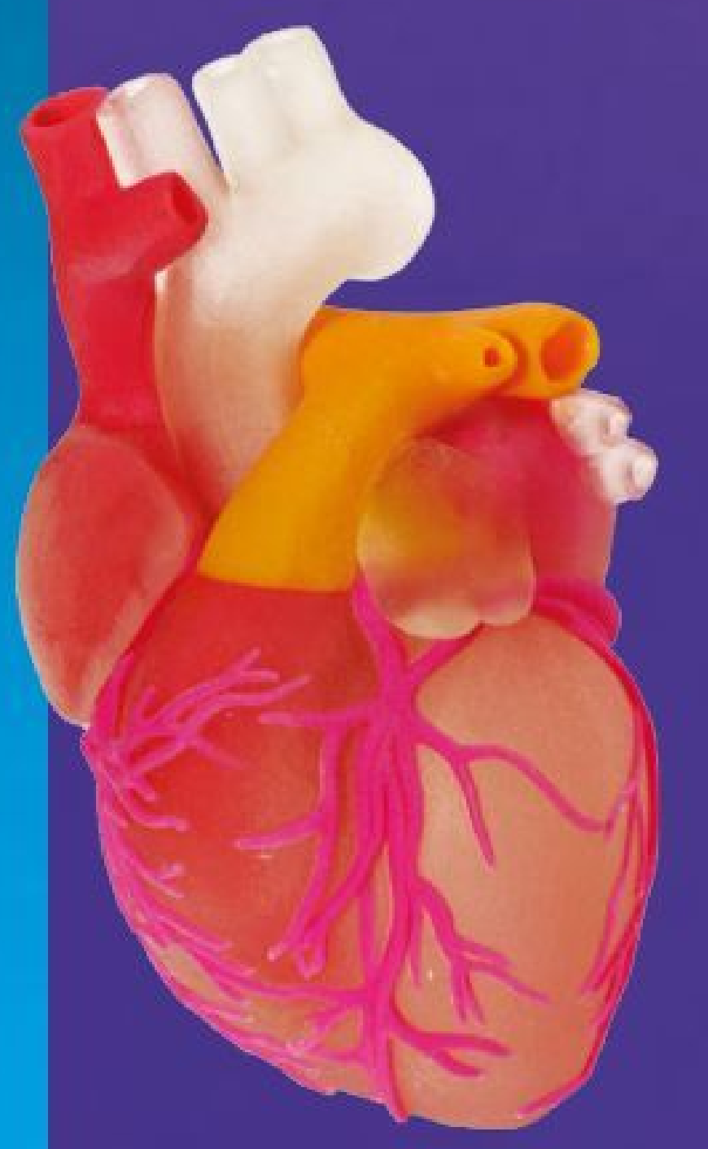

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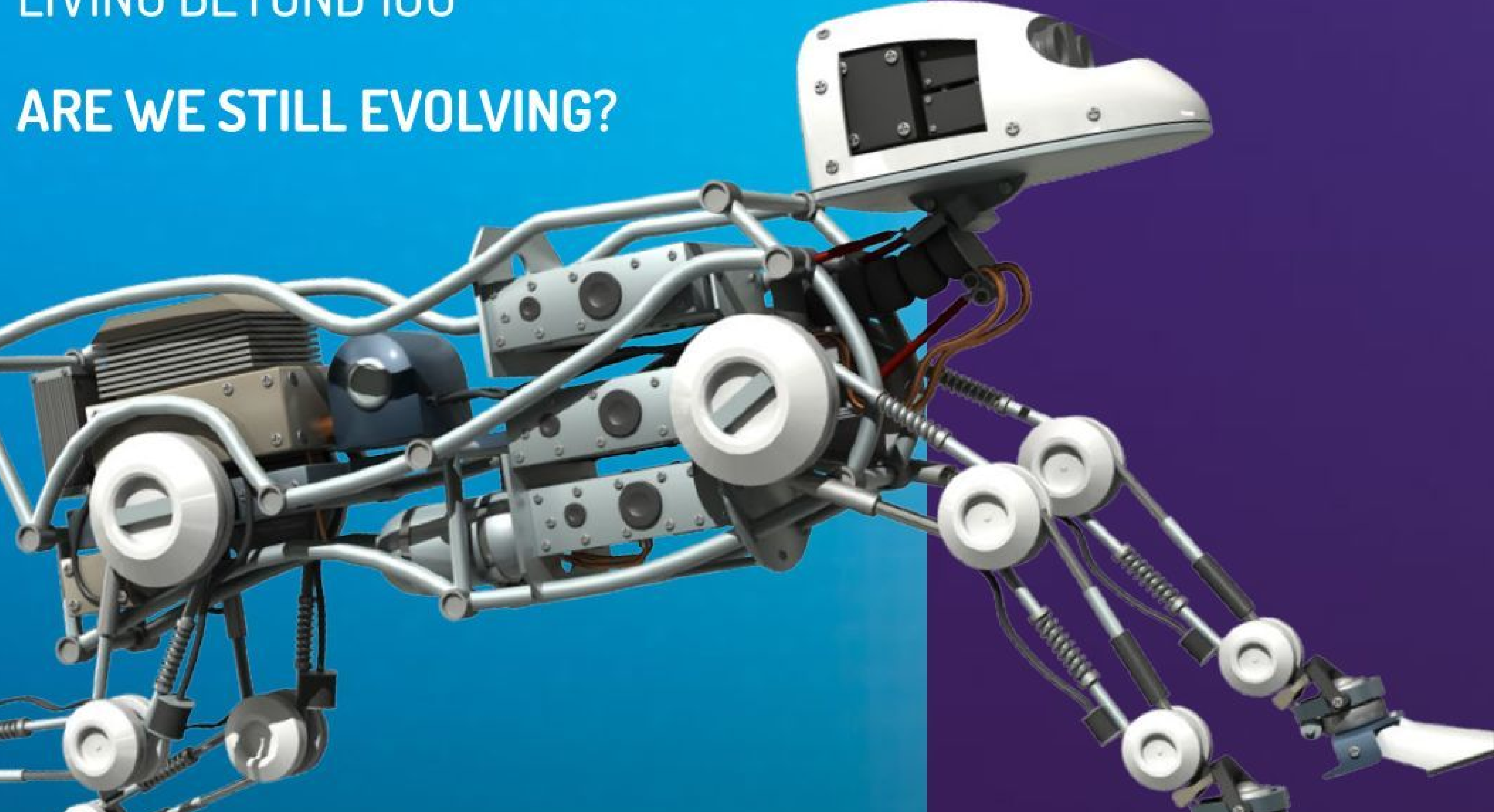

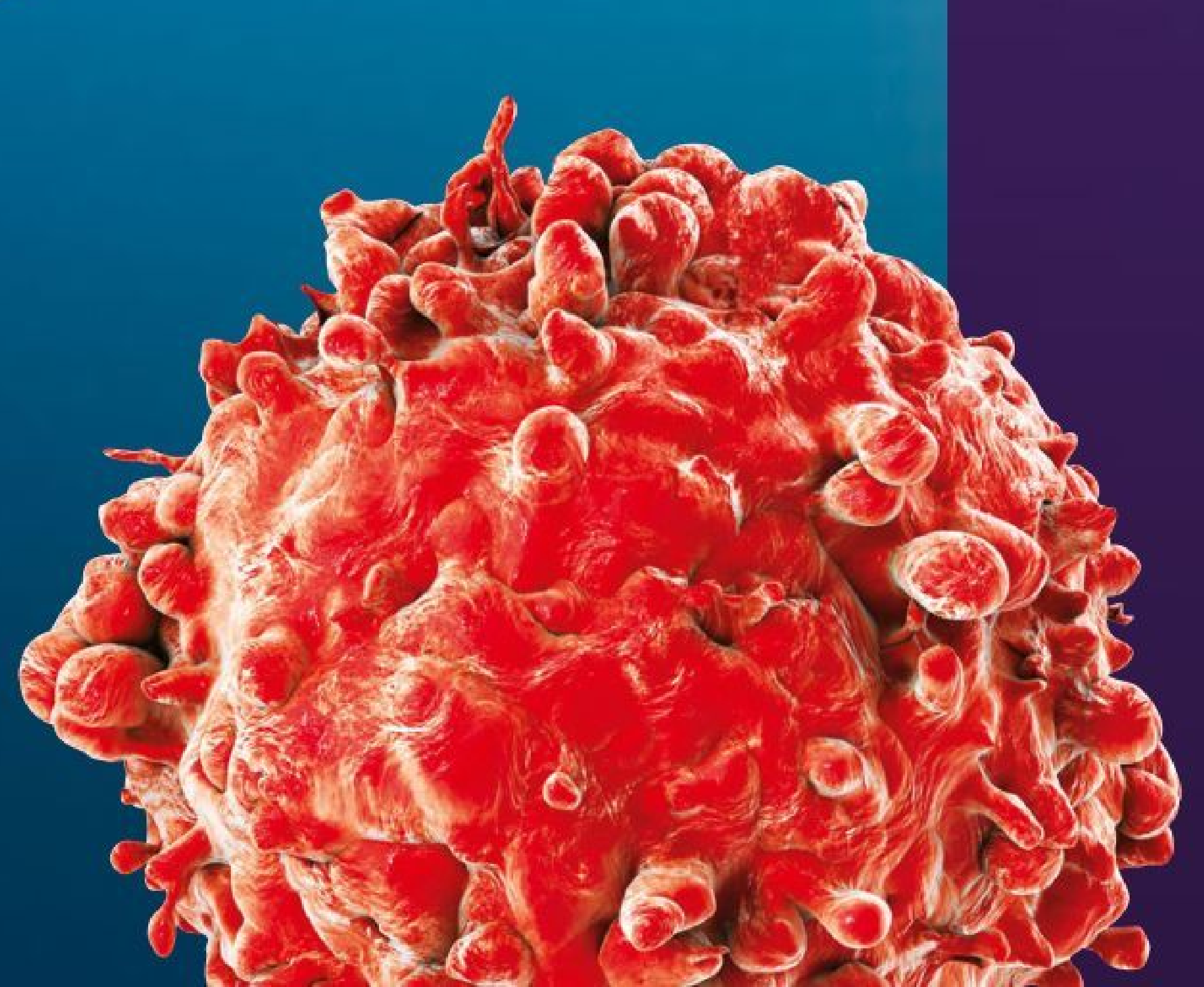

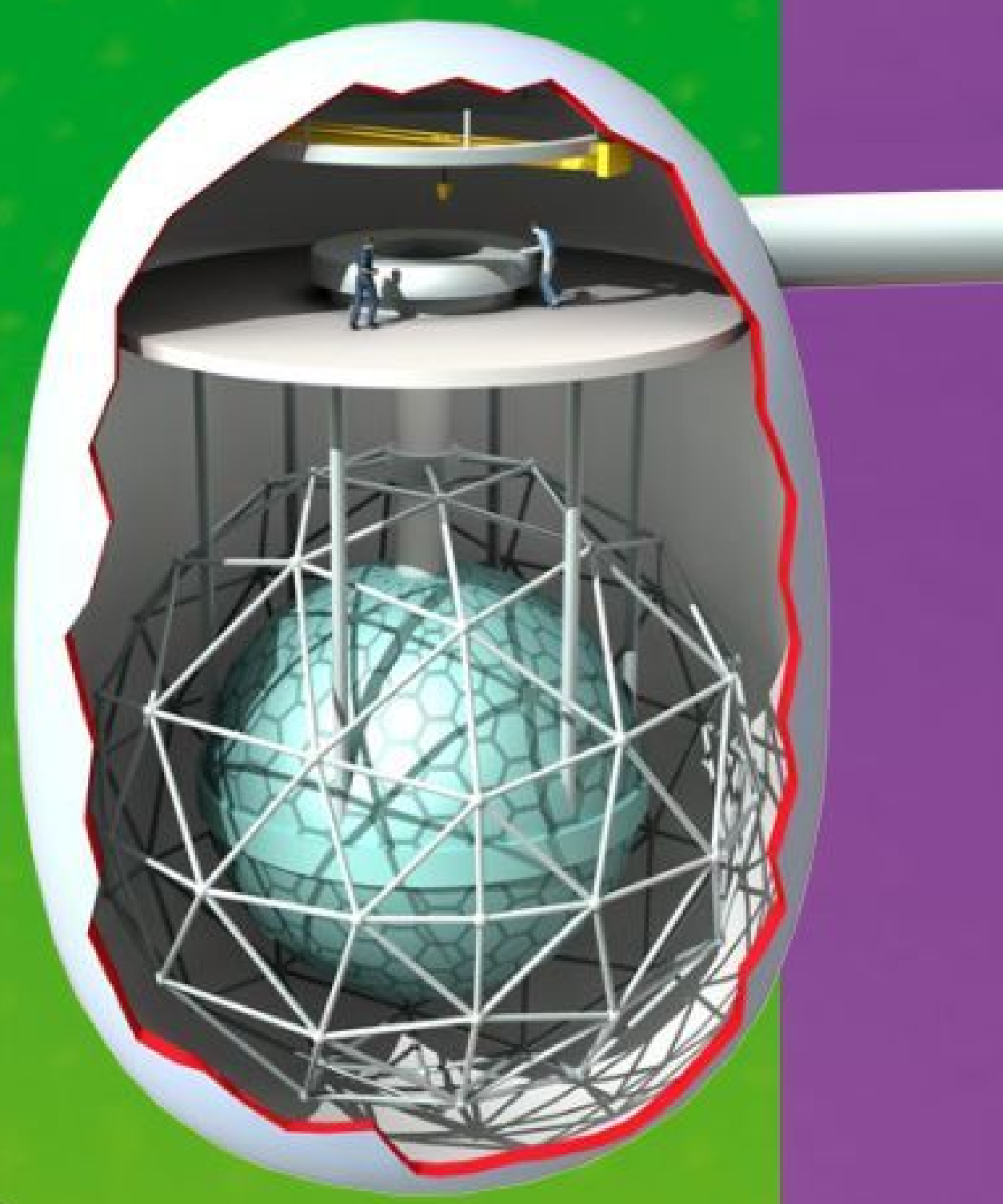

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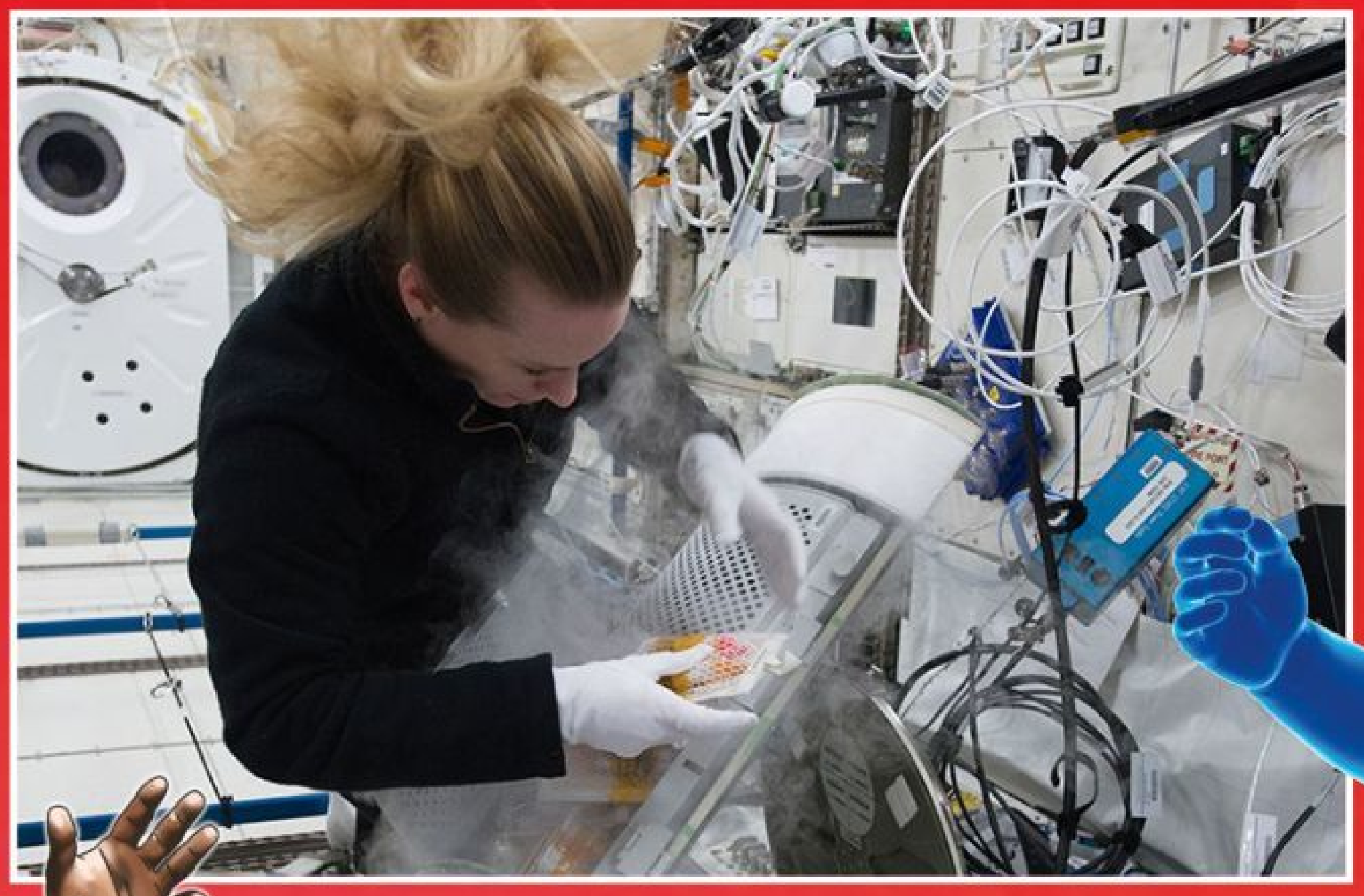

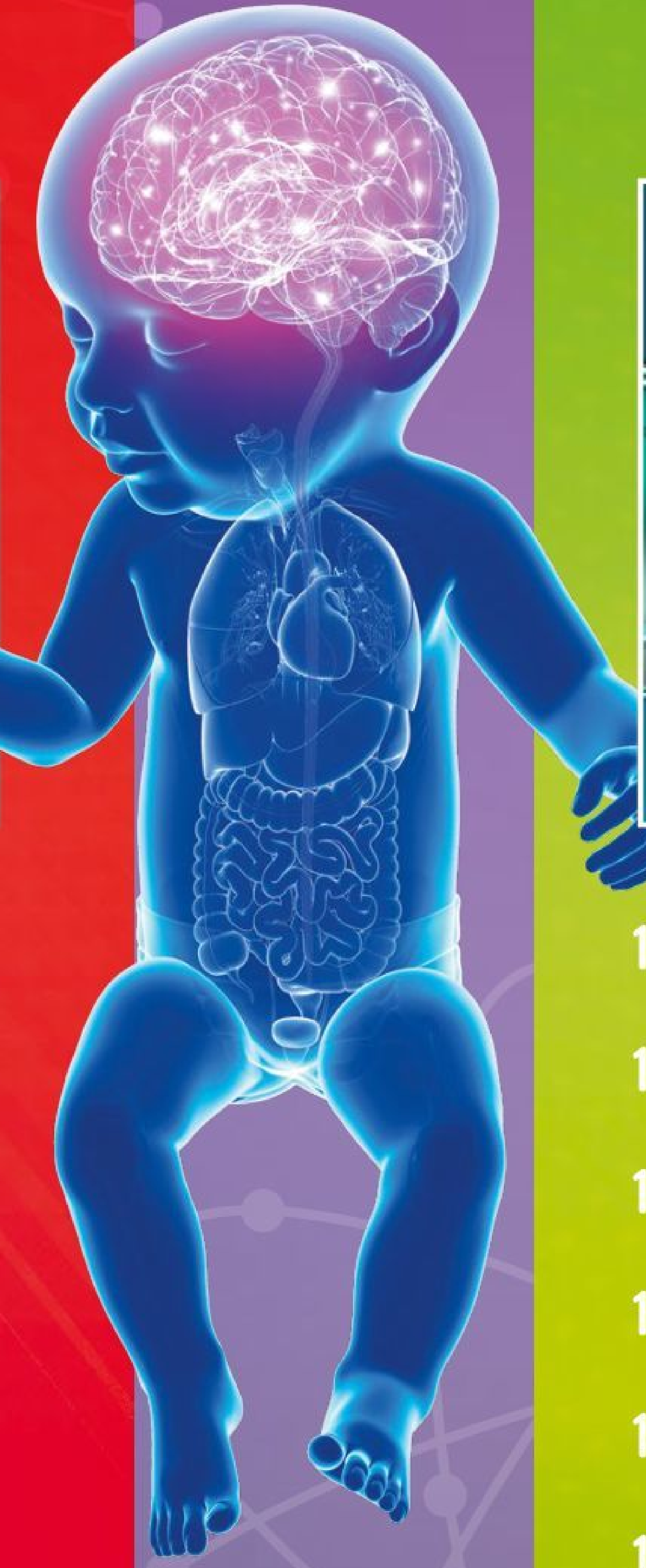

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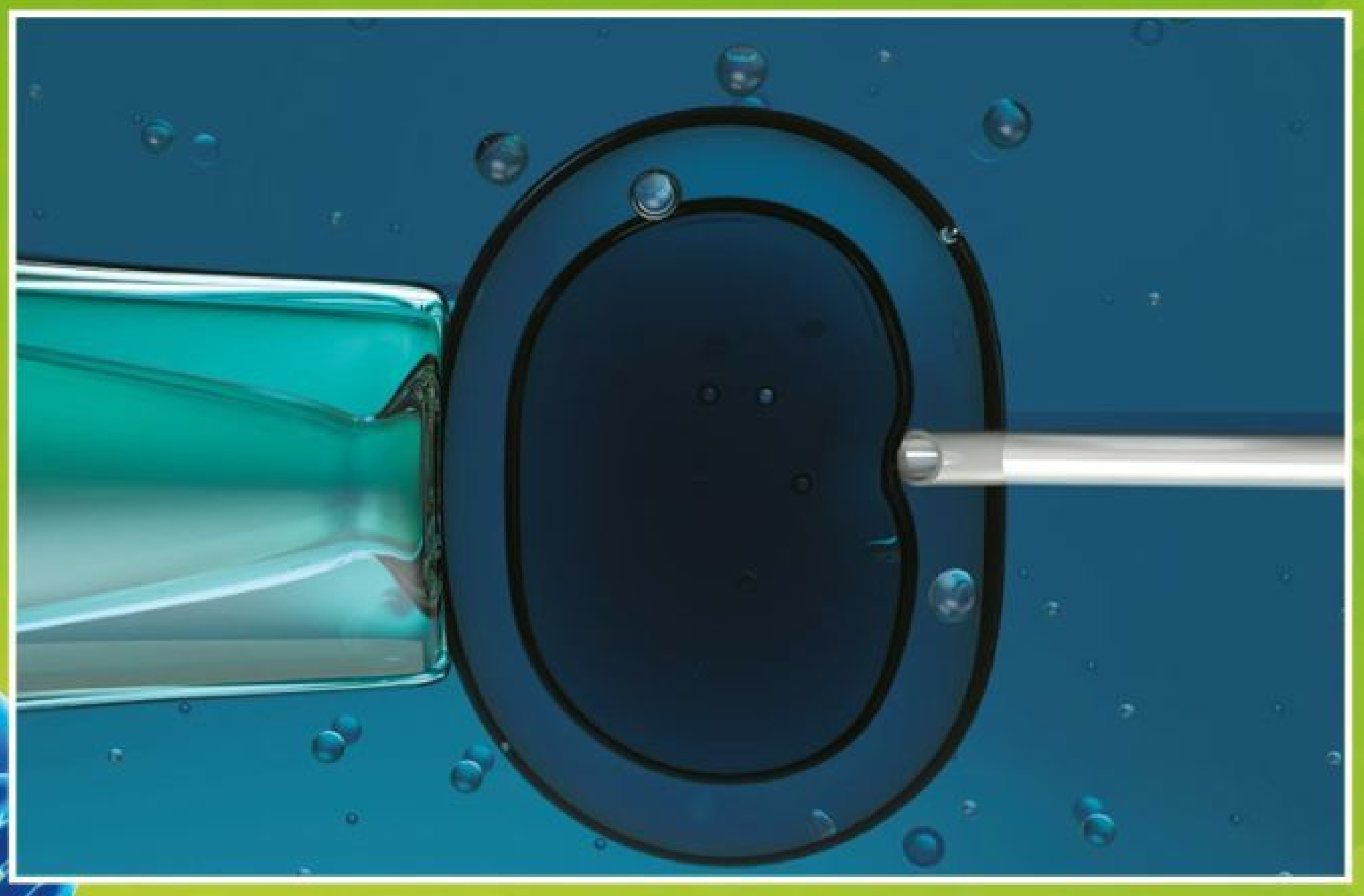

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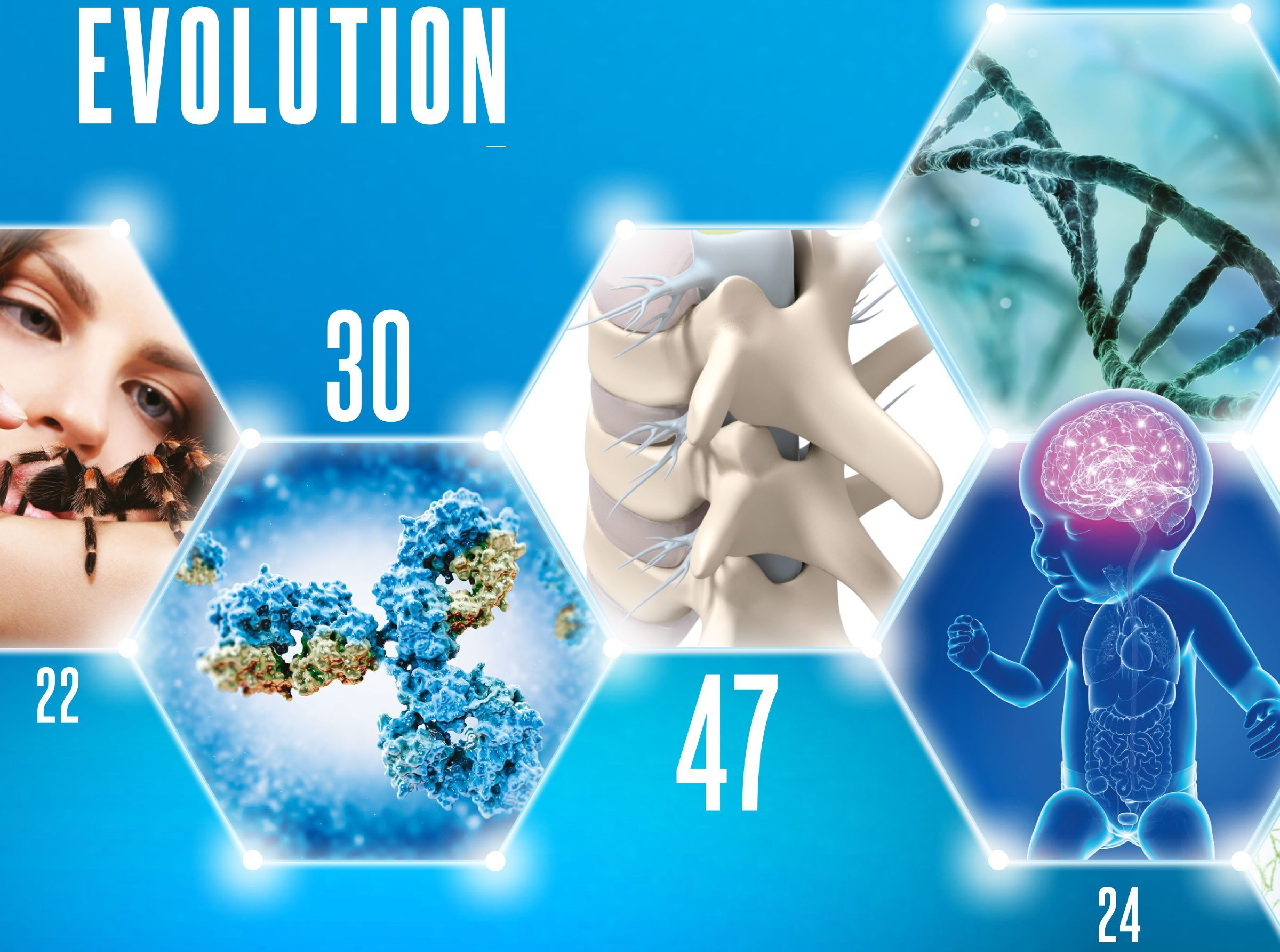
EVOLUTION



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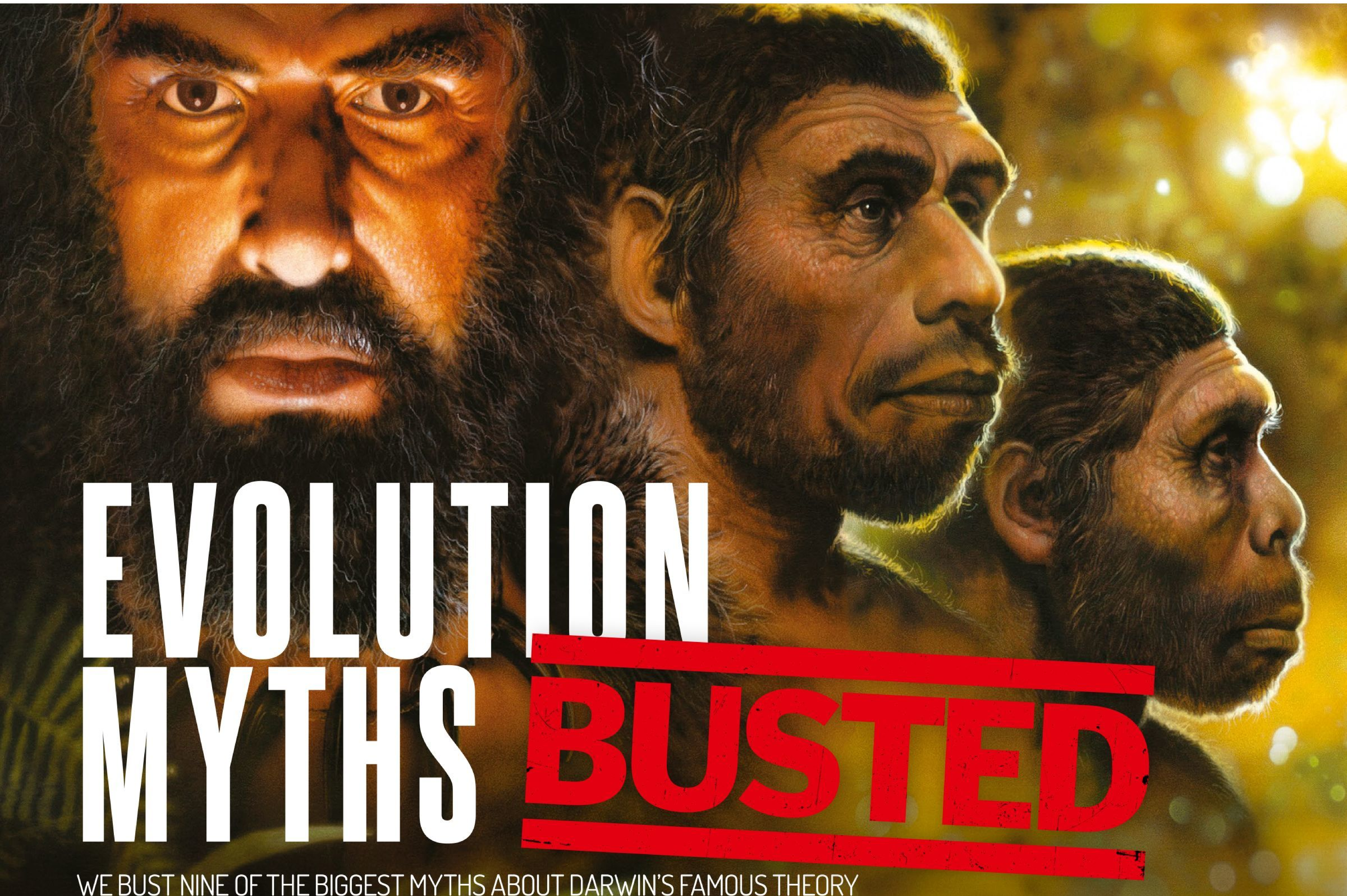


EVOLUTION MYTHS BUSTED

WE BUST NINE OF THE BIGGEST MYTHS ABOUT DARWIN'S FAMOUS THEORY

Evolution is one of the most significant scientific ideas of all time. It describes how species change over time or diverge to create more than one descendant species. It explains how humans became so brainy, why giraffes are so tall and how bacteria can develop antibiotic resistance in just days.

The race to explain the web of life started in earnest in the 1800s. For decades, naturalists had been fascinated by the similarities between different animals, and during the 19th century more and more ancient fossils were pulled from the ground. Earth scientists were beginning to reveal that the planet was much older than previously thought. It became clear that humans hadn't been around for all that long and that huge animals had once lived but were now extinct.

A naturalist called Jean-Baptiste Lamarck recognised that different species appeared to suit their environments. He proposed that they did this by adapting slowly throughout their lifetimes and then passing on these changes to their offspring. He famously thought that giraffes acquired their long necks by constantly stretching to reach the tallest trees for food and those that stretched more would have longer-necked offspring.

Although Lamarck's theory was flawed – it did not explain how the changes happened – he made two important observations: species could gradually change to better suit their environment, and these changes were passed on to future generations.

Building on these observations and his extensive studies of plants and animals, Charles Darwin published what is now known as the theory of evolution by natural selection in 1859. He proposed that, rather than adapt during their lifetimes, organisms naturally vary slightly from their relatives and that some have traits that help them to survive longer and have more offspring. Those that were best adapted would be more likely to pass their traits to the next generation, and over a long time the species would change.

At the time, Darwin didn't know quite how traits could be passed on from parent to offspring, and the theory caused a lot of controversy. However, in the decades that followed we discovered that genes were the vehicles that passed information from one generation to the next and that tiny changes in the genetic code provide the small variations that drive evolution. We have traced genetic trees, uncovered countless fossils and watched evolution happening in real time both in the wild and in the lab.

Today, the theory of evolution has been expanded and developed to become one of the key pillars of biology. Yet it still causes controversy, because it remains one of the most misunderstood areas of science. How do we know it happened if there are gaps in the fossil record? Why is it called a 'theory' if scientists know it is true? And why haven't all monkeys evolved into humans? Join us as we bust the most common myths surrounding Darwin's game-changing theory.

WE ARE DESCENDED FROM MONKEYS

SO WHY HAVEN'T ALL MONKEYS EVOLVED INTO HUMANS?

This is perhaps one of the biggest misconceptions about evolution – that humans are descended, step-by-step, from modern monkeys or apes. It may be that the well-known 'evolution of man' image, showing a series of apes that become ever-more upright and human-like, has helped to spread this myth.

First, we should be absolutely clear that monkeys and apes are not the same thing. Modern monkeys are divided into New World and Old World monkeys, both of which are separate groups of species to apes. The apes are then divided again into lesser apes (gibbons) and great apes, which include humans. So we certainly aren't descended from monkeys, but what about apes?

We share many traits with the other great apes – chimpanzees, orangutans, bonobos and gorillas – and they are our closest living relatives. But they're not our ancestors either. Each of the great apes, including humans, evolved independently from a 'common ancestor'.

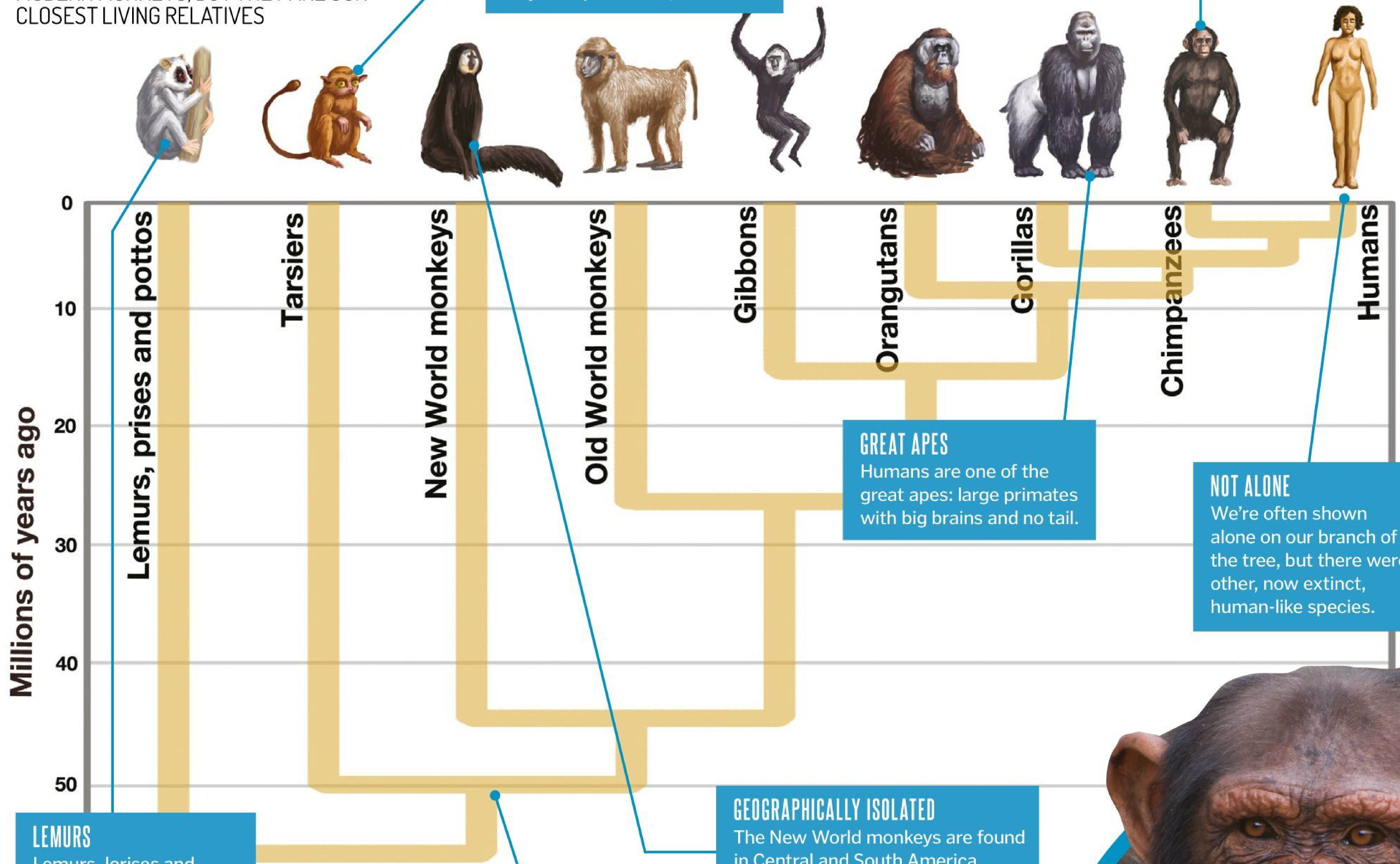
If you trace human fossils back, they gradually become more and more ape-like, with bigger teeth, smaller brains and stockier limbs. And if you trace chimpanzees back, they become more like that common ancestor too. If you go back millions of years, the evolutionary history of humans and chimpanzees eventually converges, and you will find that we share a relative that was a different species entirely – our common ancestor.

Every intersection in an evolutionary tree, like the one below, represents a common ancestor. If you trace back even further you will eventually find a common ancestor between apes and monkeys, between all primates, between all animals and so on. Each of the branches of the evolutionary tree continues to evolve, producing new species of all sizes, shapes and colours.

> "EACH OF THE GREAT APES, INCLUDING HUMANS, EVOLVED FROM A COMMON ANCESTOR"

PRIMATE FAMILY TREE

WE ARE NOT DESCENDED FROM CHIMPS OR MODERN MONKEYS, BUT THEY ARE OUR CLOSEST LIVING RELATIVES



EXTINCTIONS
There used to be tarsiers across the world, but now there are only ten species left, all in Asia.

CLOSEST RELATIVES
We are most closely related to chimpanzees and bonobos.

GREAT APES
Humans are one of the great apes: large primates with big brains and no tail.

NOT ALONE
We're often shown alone on our branch of the tree, but there were other, now extinct, human-like species.

LEMURS
Lemurs, lorises and pottos split away from other primates around 60 million years ago, and they have continued to evolve ever since.

GEOGRAPHICALLY ISOLATED
The New World monkeys are found in Central and South America, while the Old World monkeys are found in Africa and Asia.

COMMON ANCESTOR
Every intersection in the tree represents a common ancestor – a species that diverged to form two or more new species.

⬡ We are related to the other primates but not descended from them

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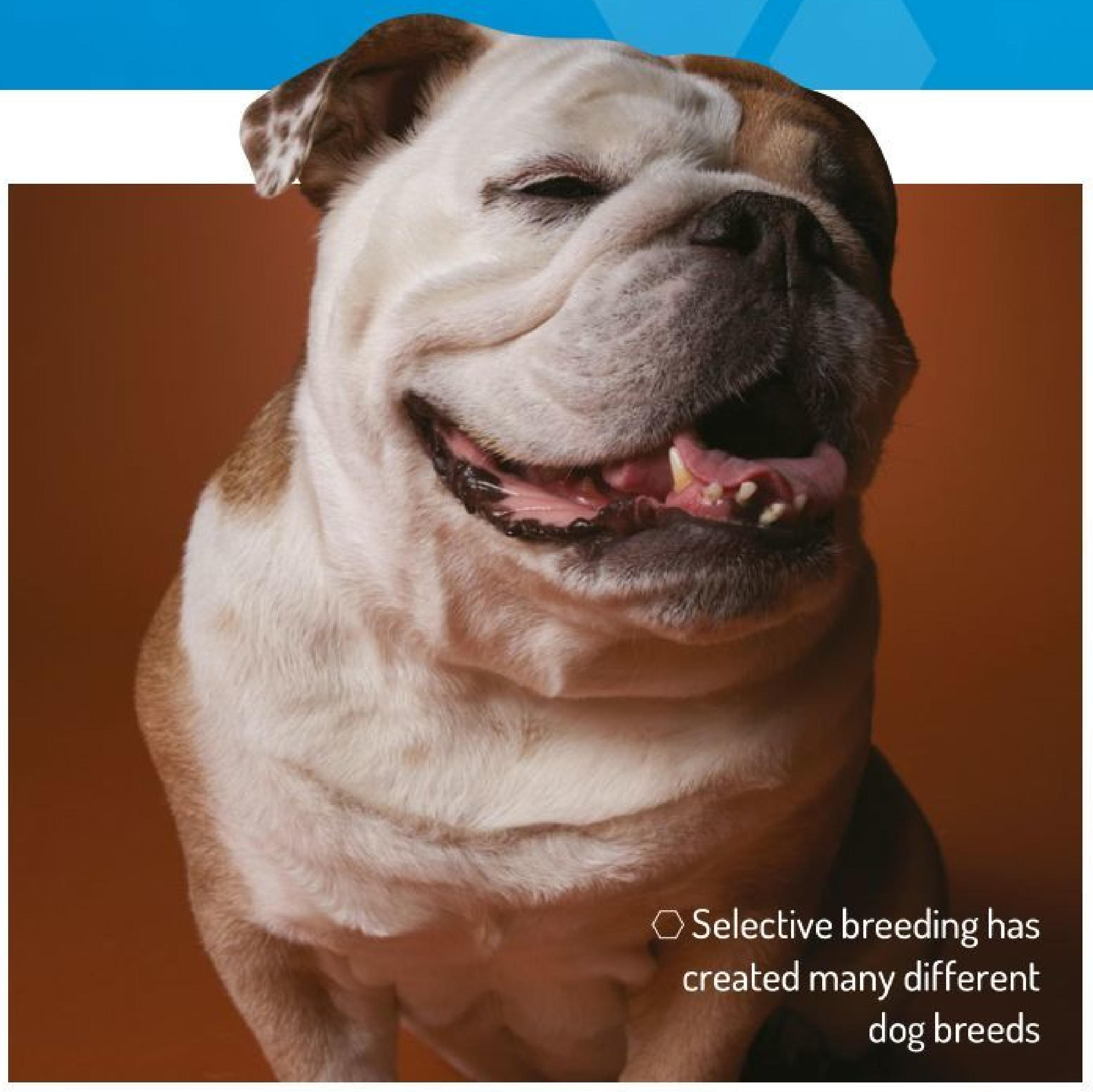
YOU CAN'T TEST EVOLUTION

IT HAPPENS SO SLOWLY THAT IT'S IMPOSSIBLE TO PROVE

Evolution usually happens over millions of years, and even in several human lifetimes we can't hope to see anything as dramatic as dinosaurs evolving into birds. The trouble with tracking evolution is that genetic changes have to be passed on for many generations before the effects become obvious. If animals live a long time, it's hard to watch them evolve before our eyes, but that doesn't mean that we can't see evolution happening in real time.

During the Industrial Revolution, Britain went through a rapid period of environmental change. Factories churned out soot, which coated the trees. Peppered moths had previously used birch trees for camouflage, and it was an advantage to be pale, because dark moths stood out against the bark and were quickly spotted and eaten by birds. But, once the soot came, being darker became an advantage. Quickly, the number of darker moths in the population grew as they survived and passed on their useful genetic trait.

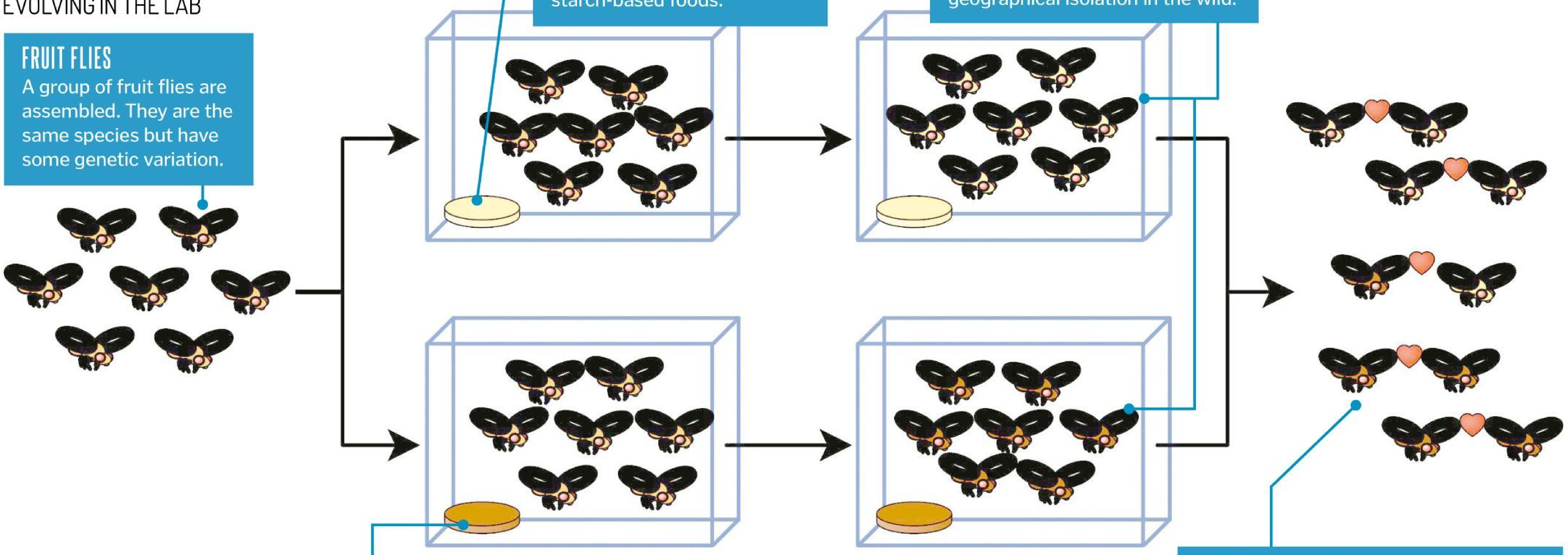
If you want an example in your own back garden, we have been simulating evolution with dogs for centuries. We choose which traits we like and only breed the dogs that have them: hounds have been selected for scent and sight; herding dogs were bred for double coats that shield them from the weather; and bulldogs were favoured for their flattened faces. This human-made canine evolution is still happening today, and you only have to look at the emerging health problems with pure breeds to see the effects in action.



⬡ Selective breeding has created many different dog breeds

EVOLUTION IN ACTION

INSECTS AND MICROBES REPRODUCE SO FAST THAT IT'S EASY TO SEE THEM EVOLVING IN THE LAB



FRUIT FLIES
A group of fruit flies are assembled. They are the same species but have some genetic variation.

STARCH
Half of the group is separated into a cage containing starch-based foods.

MALTOSE
The other half of the group is put into a cage containing maltose-based foods.

SEPARATION
The flies are kept separate for several generations, mimicking geographical isolation in the wild.

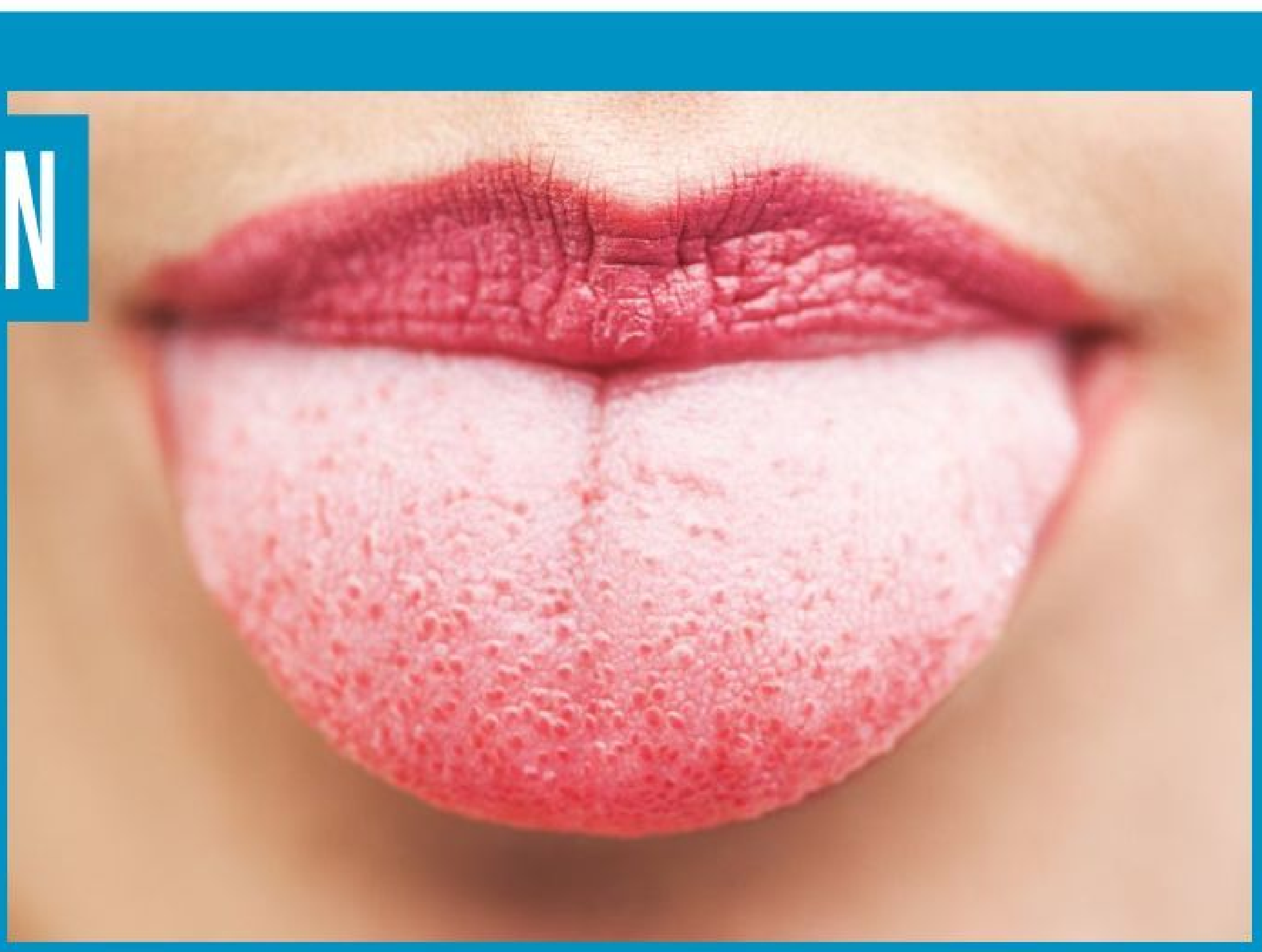
REINTRODUCTION
When the two groups are reunited, maltose flies prefer to mate with other maltose flies, and starch with starch – this is an early stage of the flies evolving into two different species.

> "Evolution has no goal at all, and the results are far from perfect"

EVERYTHING IS AN ADAPTATION

ALL TRAITS HAVE AN EVOLUTIONARY PURPOSE

It's tempting to imagine that there is a story behind every trait, but not everything is an adaptation. Much of what you see today happened by chance or as a side-effect of something else that turned out to be useful. Others are just remnants of traits that used to be useful but are not really needed any more. Evolution often involves trade-offs and compromises, and it is constrained by the adaptations that an organism already has.



CHANCE MUTATIONS
Many traits don't have an obvious reason or advantage and aren't an adaptation. For example, around 25 per cent of the population are 'supertasters', with far more taste buds than others.

SIDE-EFFECTS
Some traits are side-effects of others. The colour of our blood isn't an adaptation; instead, it is a side-effect of the molecule that transports oxygen – haemoglobin just happens to be red.

EVOLUTION EXPLAINS THE ORIGINS OF LIFE

IF EVOLUTION EXPLAINS HOW LIFE HAS CHANGED, SURELY IT SHOULD EXPLAIN HOW IT ALL BEGAN

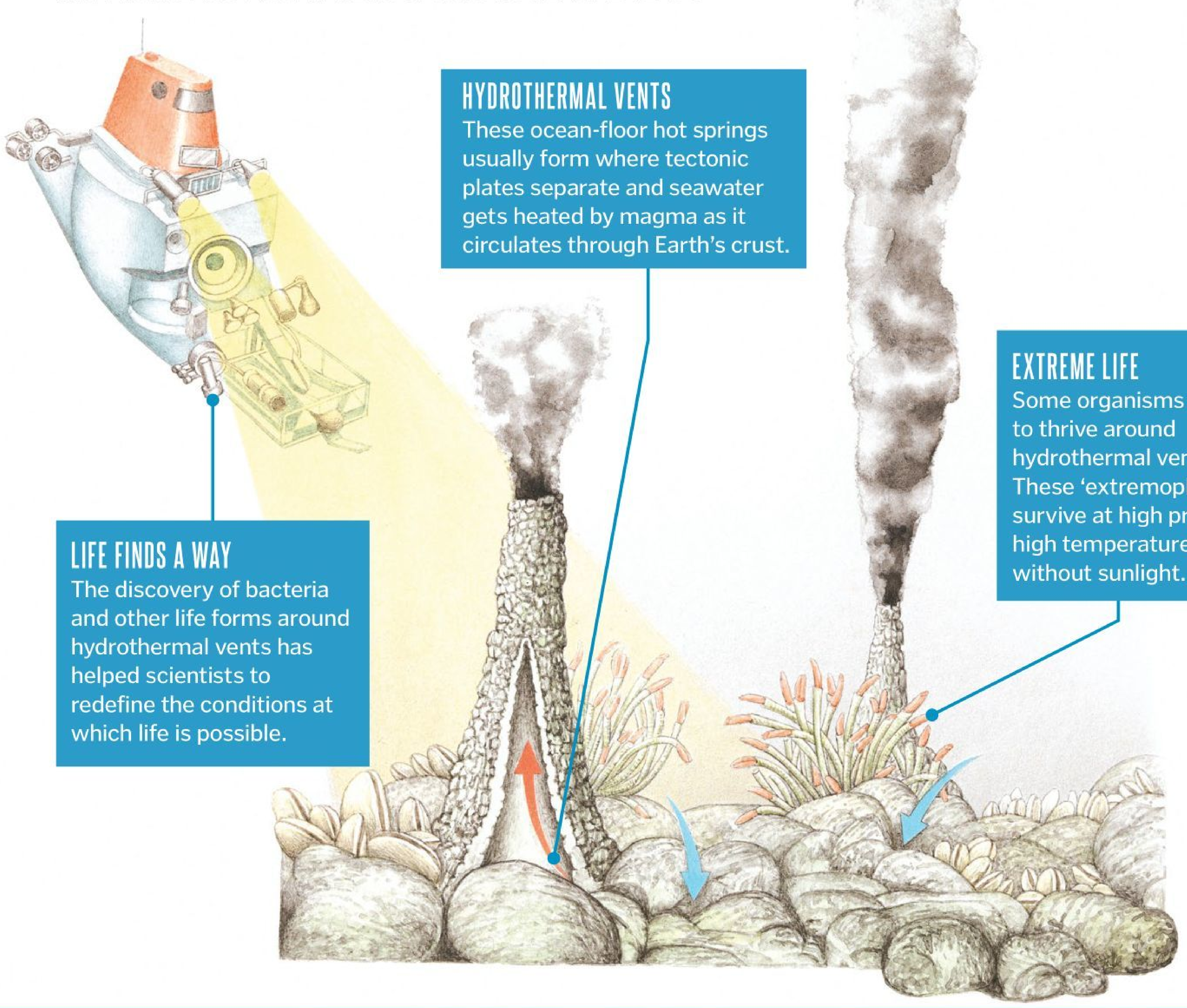
Evolution can tell us a lot about why life is the way it is and how life changes and adapts over time, but it doesn't claim to explain how it started.

Evolution has already taken us back as far as LUCA: the Last Universal Common Ancestor. This is the organism from which all life on Earth evolved. Using gene tracking and comparing the genes of organisms in the two most ancient branches of the tree of life (archaea and bacteria), it is estimated that LUCA lived around 3.8 billion years ago and had at least 100 genes.

The science of evolution can give us clues about what would have been needed for life to begin, but this puzzle has yet to be solved and is currently being tackled by a range of scientists working across biology, chemistry and the Earth sciences. But, however life began, evolution explains what happened next.

PRIMITIVE LIFE

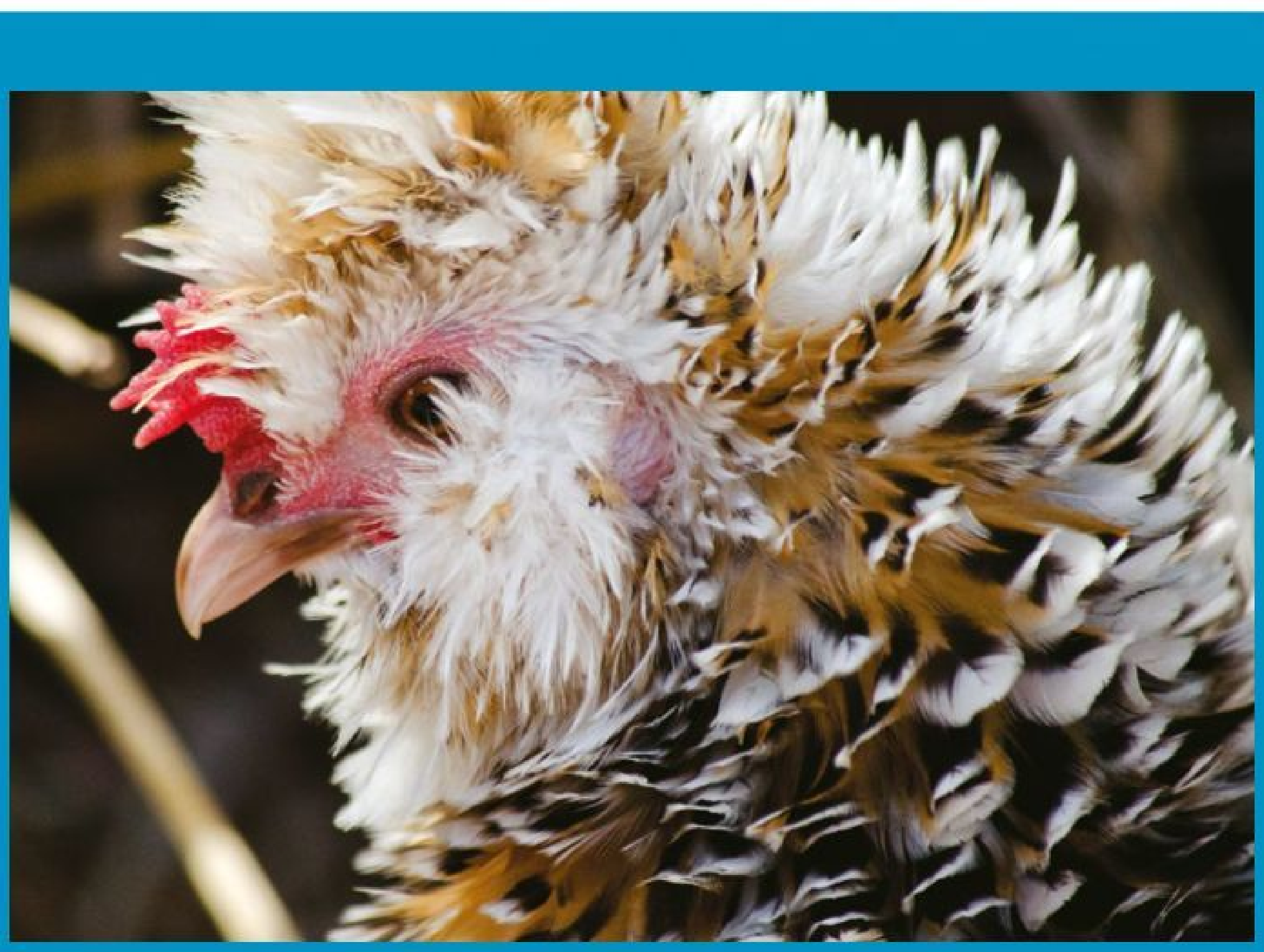
ONE OF THE MOST COMPELLING IDEAS IS THAT LIFE BEGAN IN THE WARM, MINERAL-RICH WATERS OF HYDROTHERMAL VENTS



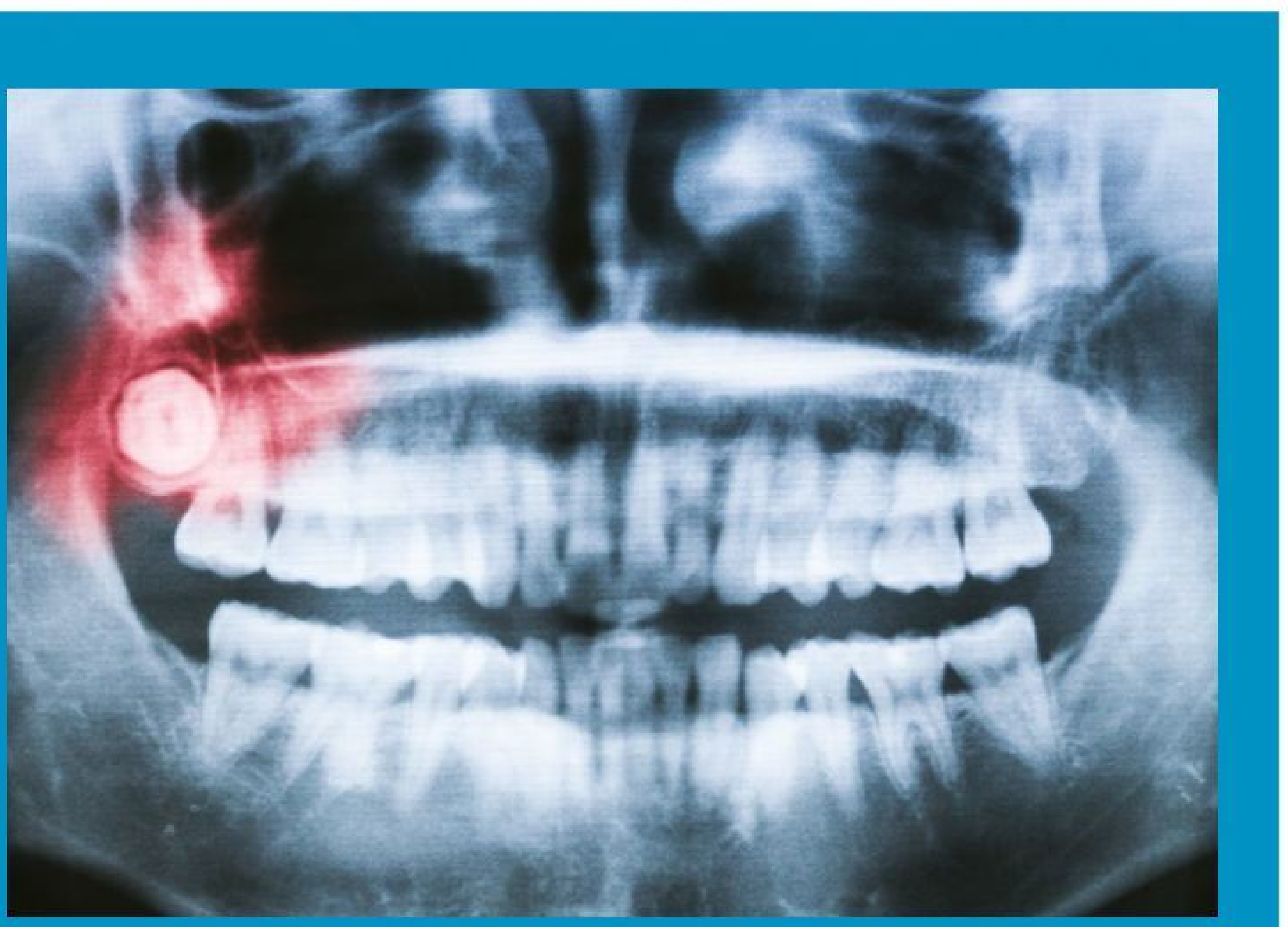
HYDROTHERMAL VENTS
These ocean-floor hot springs usually form where tectonic plates separate and seawater gets heated by magma as it circulates through Earth's crust.

EXTREME LIFE
Some organisms seem to thrive around hydrothermal vents. These 'extremophiles' survive at high pressure, high temperatures and without sunlight.

LIFE FINDS A WAY
The discovery of bacteria and other life forms around hydrothermal vents has helped scientists to redefine the conditions at which life is possible.



MULTIPURPOSE GENES
Many genes have more than one function (known as pleiotropy). For example, these curly feathered chickens have one gene change that affects their digestion, body temperature and egg laying, as well as their feathers.



VESTIGIAL TRAITS
Some traits are left over from our ancestors and are no longer useful. Take our wisdom teeth; they were useful when our jaws were bigger and diets tougher but now they're often just a nuisance.

EVERYTHING HAPPENS FOR A REASON

EVOLUTION HAS AN ULTIMATE GOAL AND IS TRYING TO SOLVE A PROBLEM

The way we talk about evolution can make it seem as though organisms are trying to evolve to be better, faster or stronger than the rest. In truth, evolution has no goal at all and the results are far from perfect.

Evolution is ultimately driven by genetic mutations, which happen fairly randomly. Some of these variations help organisms to survive a little bit longer or have more offspring, and these useful genes are passed on to the next generation. Others make life a little harder.

The environment and conditions that organisms find themselves in dictate which of these random mutations will be useful and which won't. This could be down to the climate, predators, food availability or attractiveness to a mate, but however the traits are selected, they make gradual changes over time with no end goal in sight.

Evolution works by trial and error, and the end results aren't always as polished as they could be. For example, the human eye has a serious flaw. The blood vessels and nerves actually run in front of the light-detecting cells, and have to travel through the back of the eye to get to the brain. This creates a blind spot. It is a step-by-step process that has led to our eyes evolving, but it certainly isn't the 'best' way things could have been arranged.

Organisms don't want, try or need to evolve, they just do – and the results are both amazing and unpredictable.

© WIKI; Thinkstock

THE EYE IS TOO COMPLEX TO HAVE EVOLVED

HALF OF THE HUMAN EYE IS OF NO USE, SO HOW COULD THESE INTRICATE VISUAL MACHINES HAVE DEVELOPED?

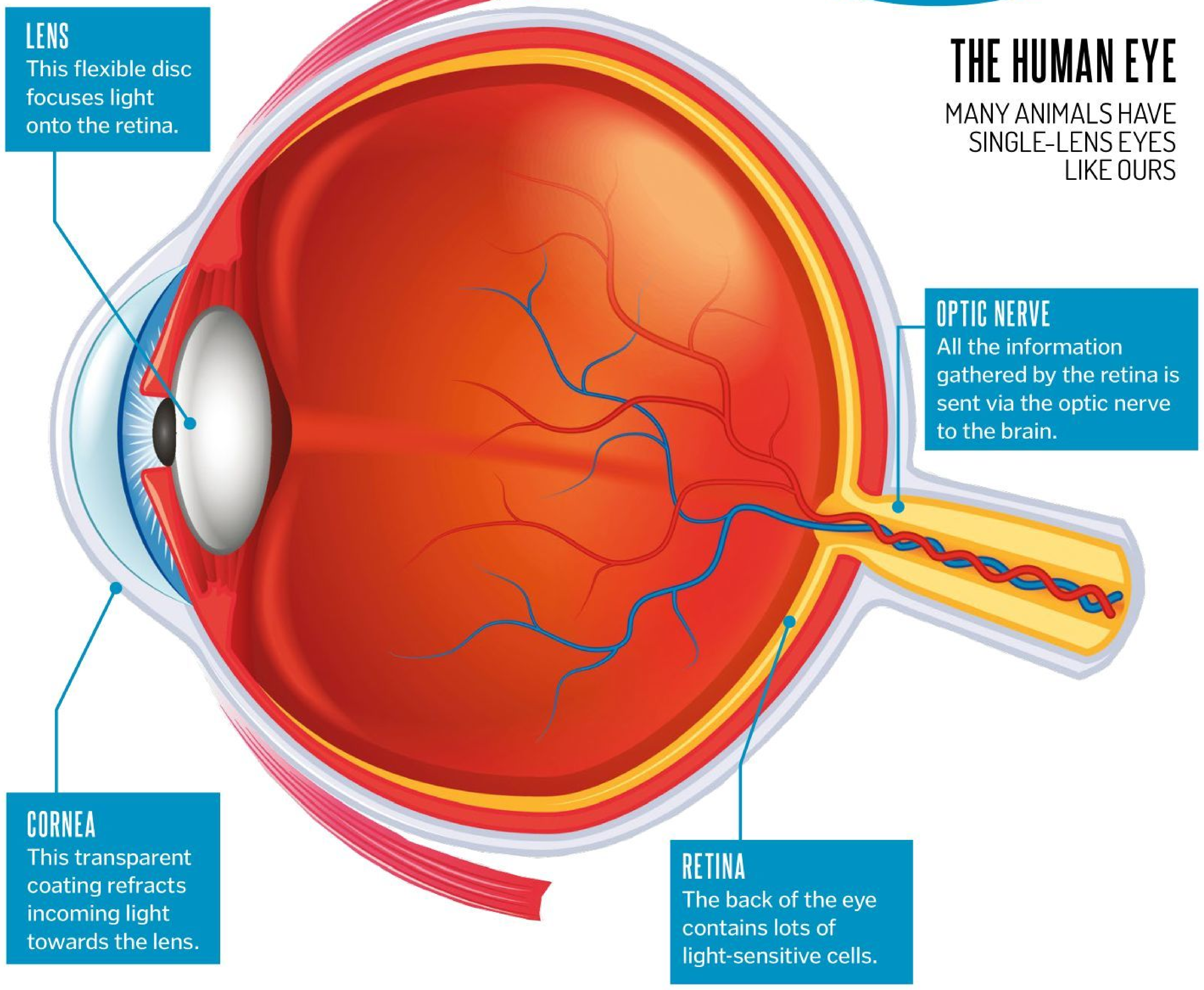
Even Darwin had trouble imagining that eyes were the product of evolution, but if you take it step by step, it starts to make sense.

At the simplest level, eyes are spots or patches of pigments that respond to sunlight. If these pigments are on a flat surface, they just sense light and dark, but if they become dipped down into pits, they can be used to tell which direction the light is coming from. Then, if these pits become a little deeper, and the opening starts to close over, it forms the equivalent of a pinhole camera, restricting the light coming in and producing actual images. If that pinhole then becomes covered by a layer of transparent cells, the pit can fill with fluid, allowing a lens to start to form from crystals inside. This lens helps with focusing, making the images even sharper.

Each of these small adaptations may give an organism a slight advantage in its environment, such as being able to hunt more effectively or spot predators from further away. Over many generations the adaptation is selected for, and the eye shape of the species gradually changes.

THE HUMAN EYE

MANY ANIMALS HAVE SINGLE-LENS EYES LIKE OURS



LENS
This flexible disc focuses light onto the retina.

OPTIC NERVE
All the information gathered by the retina is sent via the optic nerve to the brain.

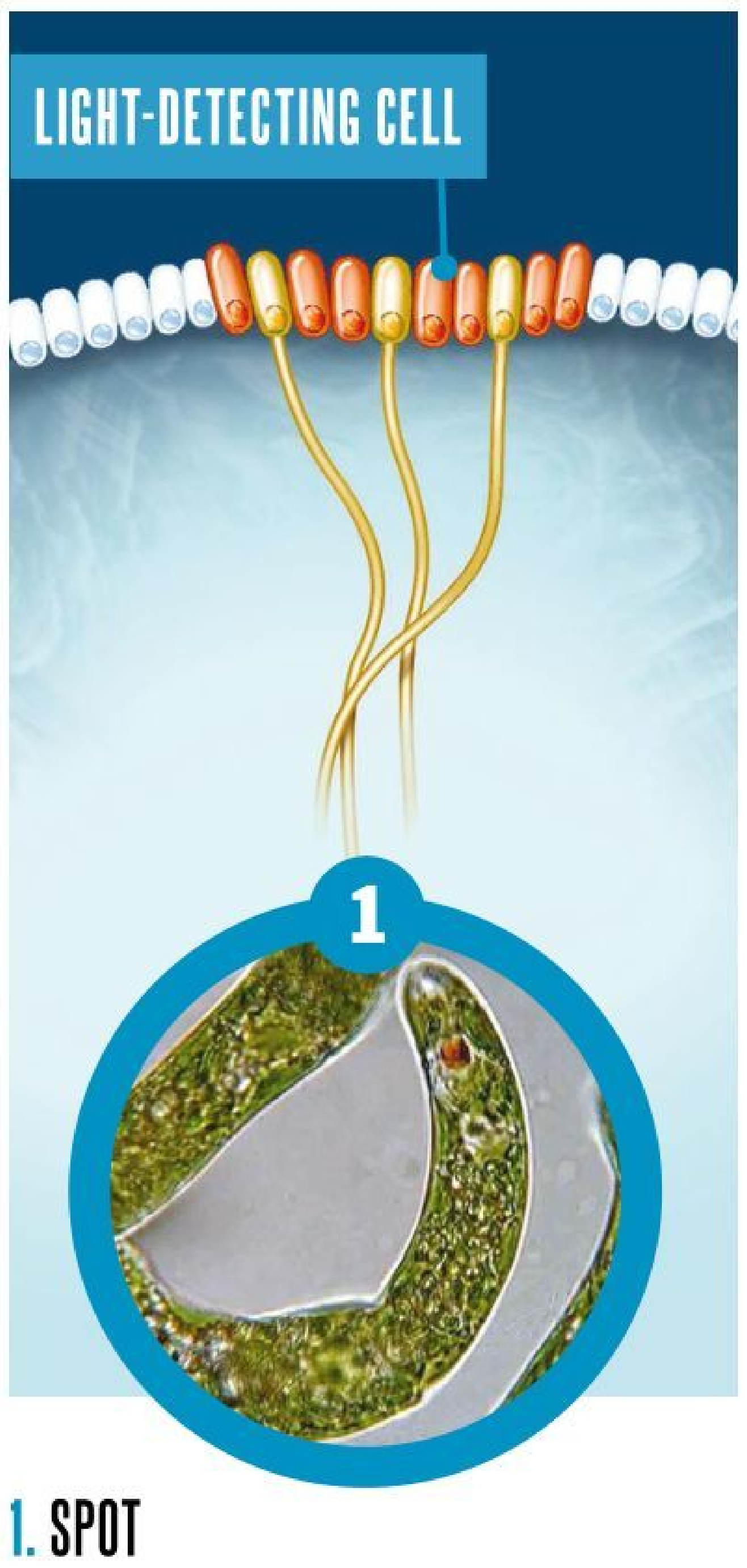
CORNEA
This transparent coating refracts incoming light towards the lens.

RETINA
The back of the eye contains lots of light-sensitive cells.

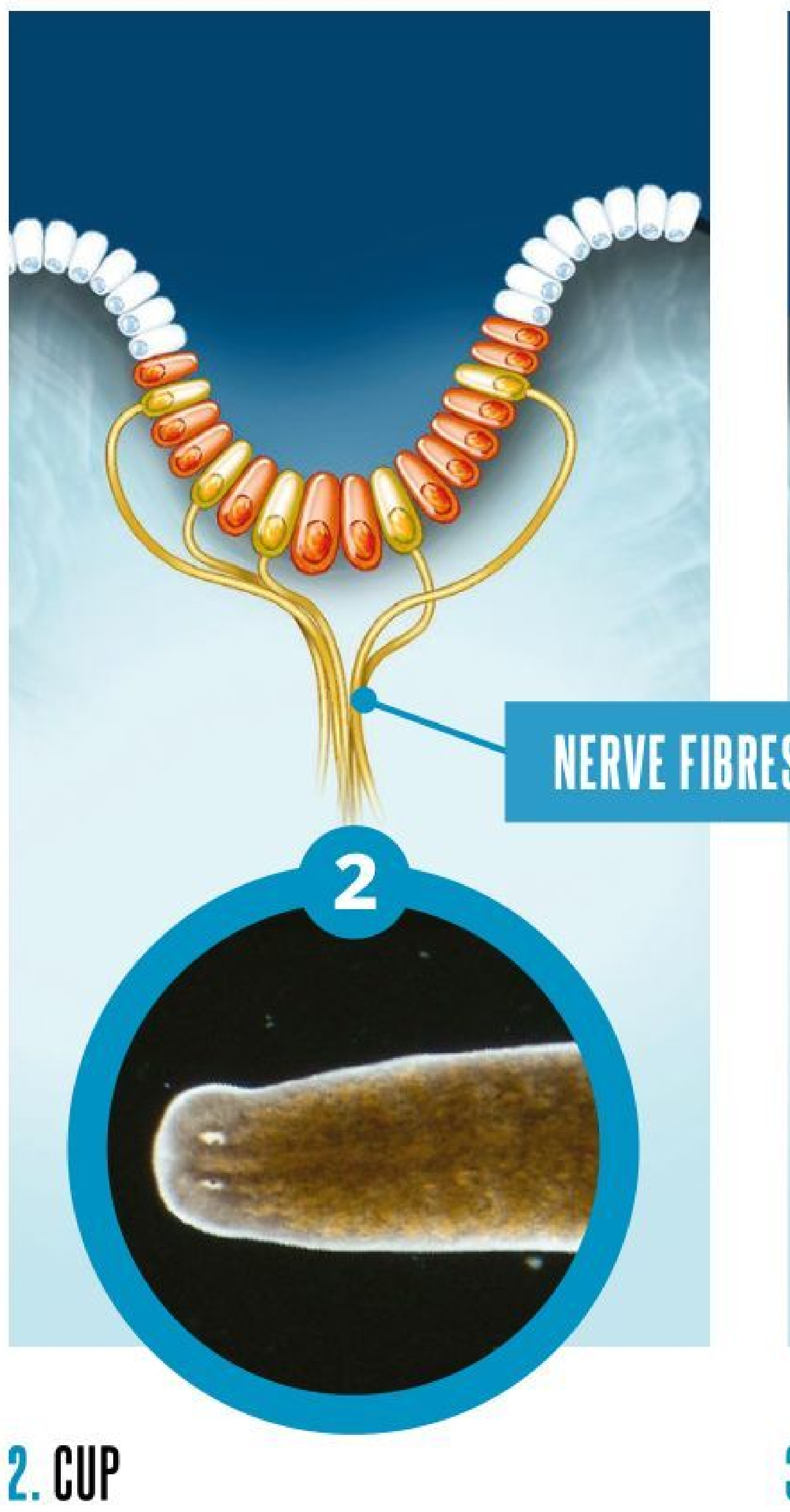
INCREASING COMPLEXITY

IF YOU LOOK CLOSELY, SIMPLE VERSIONS OF THE HUMAN EYE EXIST IN THE NATURAL WORLD

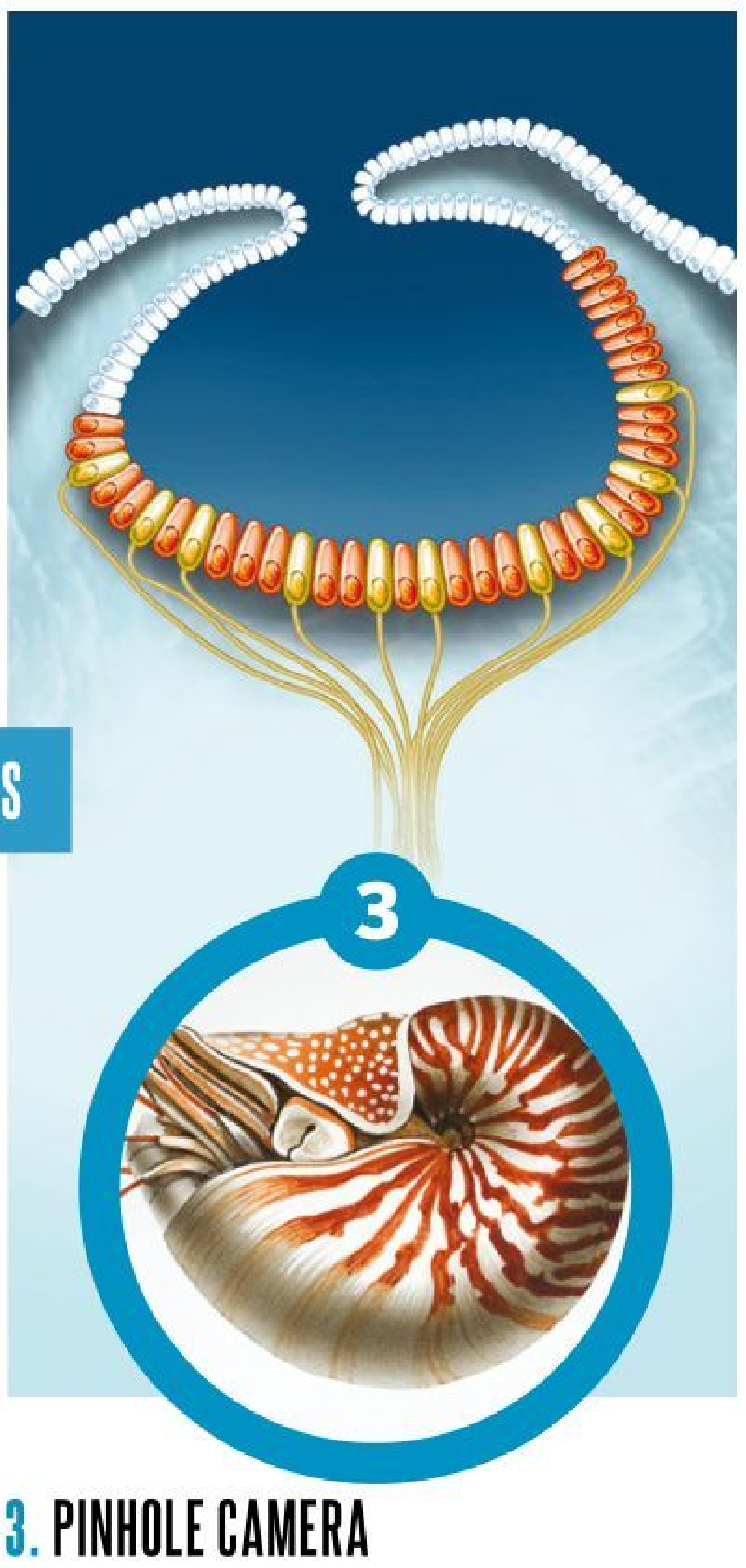
> *"Those with the most useful adaptations are more likely to survive and breed"*



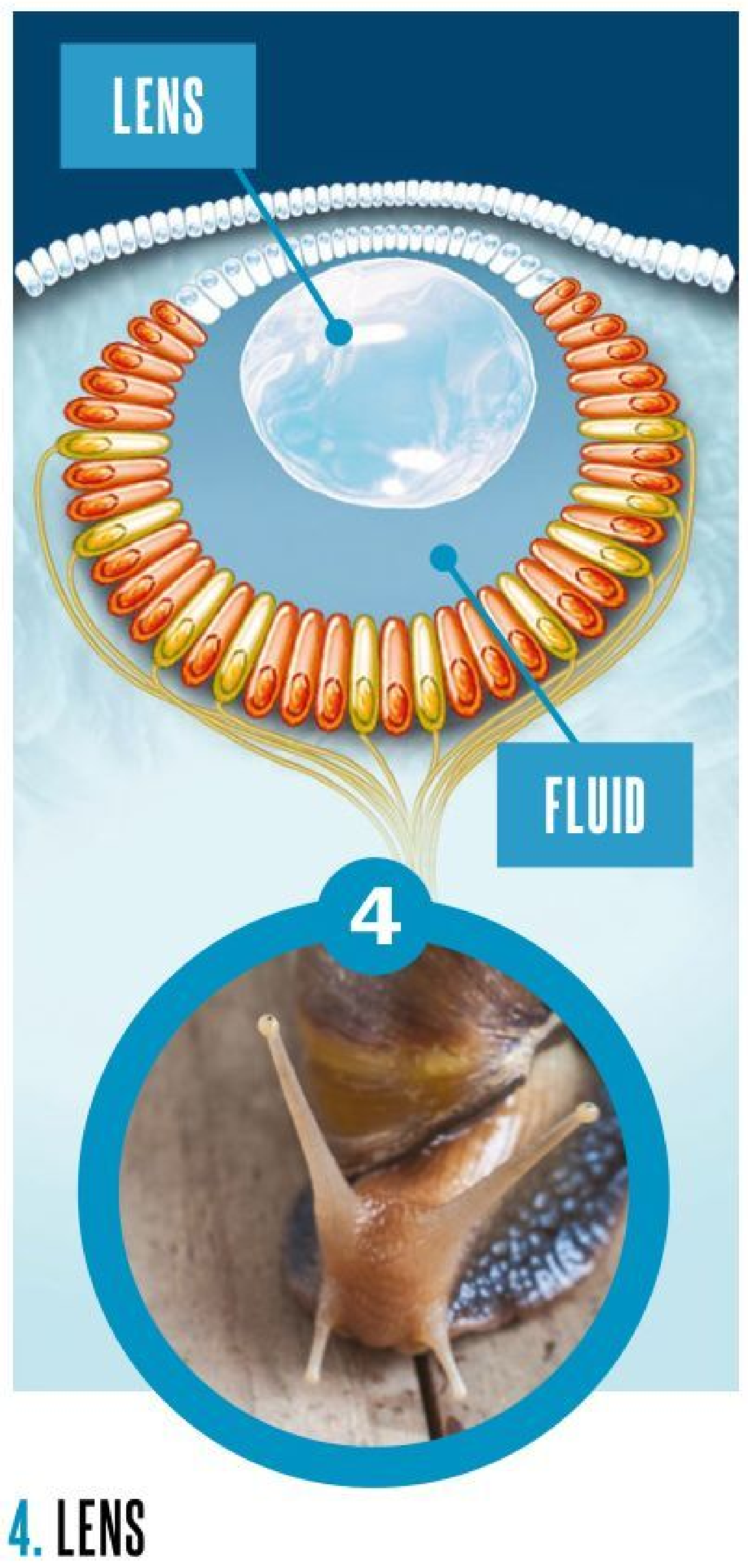
1. SPOT
Single-celled organisms called euglena have 'eyespots' containing light-sensitive pigments that help them to detect light and dark.



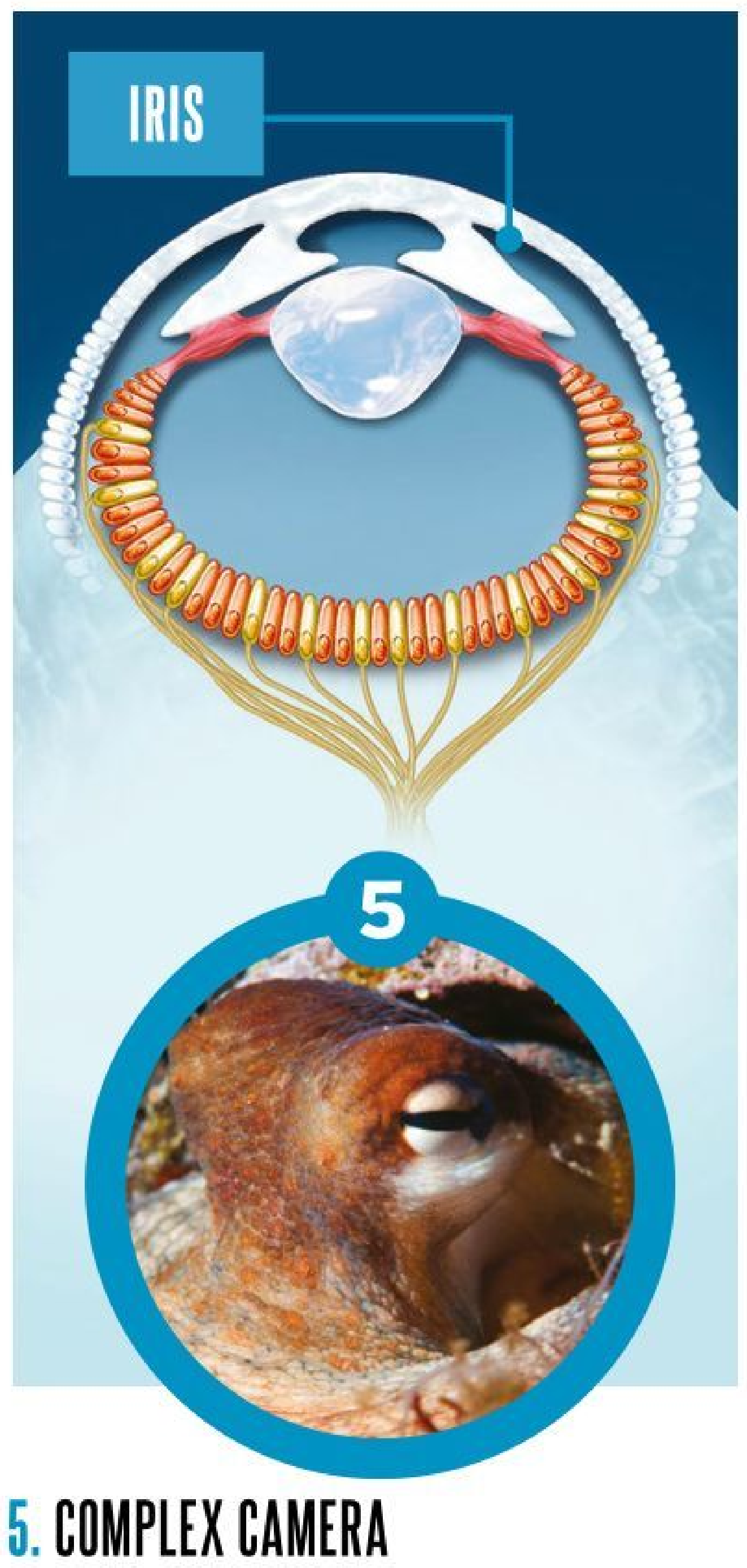
2. CUP
Flatworms have spots of pigment that are buried inside cups, helping them to determine which direction the light is coming from.



3. PINHOLE CAMERA
Deeper cups with a slightly closed opening form the equivalent of a pinhole camera, allowing animals like the nautilus to see images.



4. LENS
Transparent cells cover the opening at the front of the eye, and a simple lens structure forms inside. Snails have eyes like this.



5. COMPLEX CAMERA
Over time, tiny improvements gradually add up to the complex camera eyes that organisms such as octopuses and humans have today.

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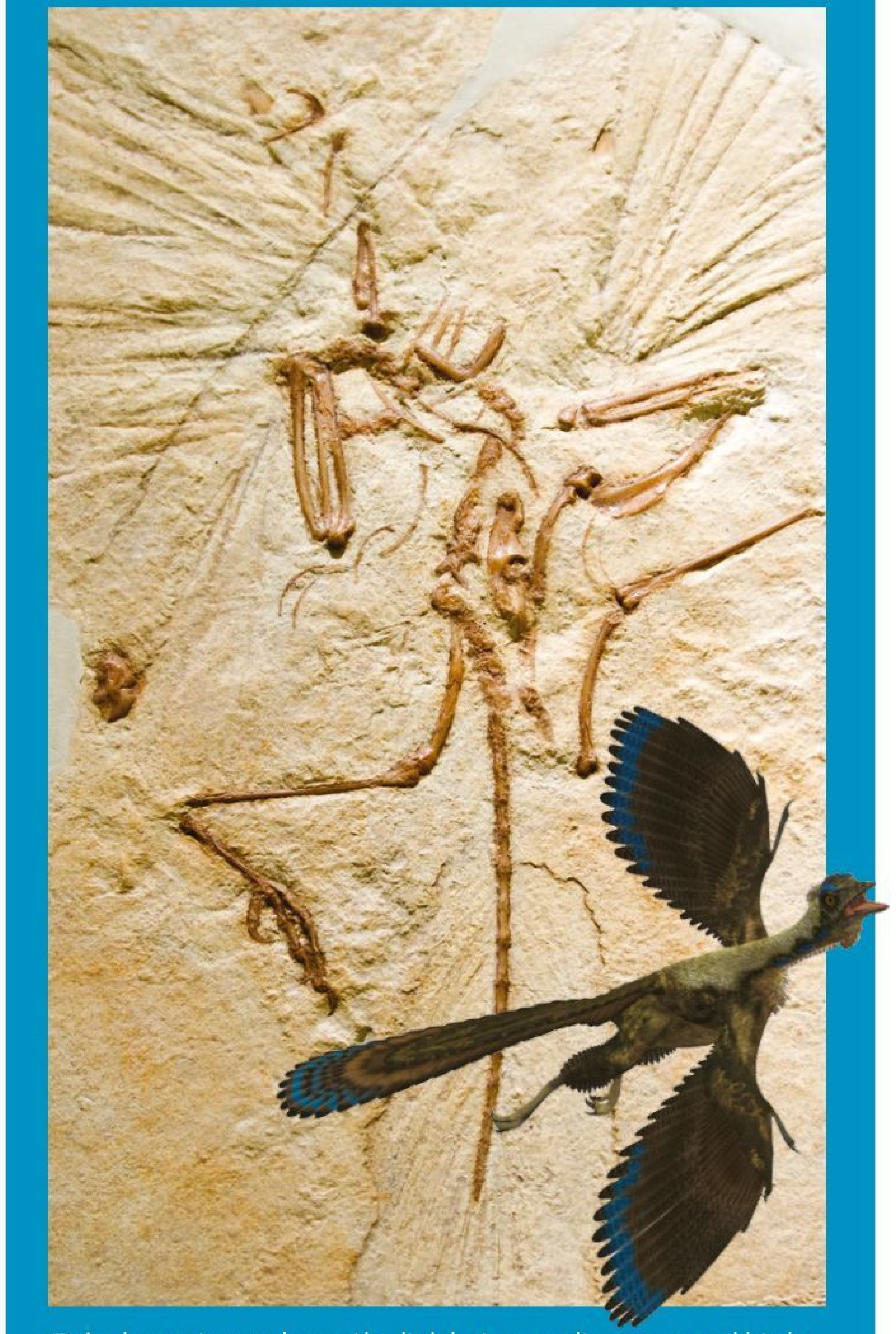
AREN'T THERE GAPS IN THE FOSSIL RECORD?

MISSING LINKS IN FOSSILS MUST DISPROVE EVOLUTION

It would be nice if we could see neat historical lines that traced the evolution of modern species step by step, but fossils are very rare. Of all of the mammal species that are currently in danger of extinction, we only know of fossils for nine per cent of them. In the future, if we were to look back, it would be like the rest never existed at all.

Fossils don't form very often. Even for those animals with the right body type, fossil formation is very dependent on how – and where – they die. In jungles, for example, other organisms quickly devour the dead, removing all traces of their bodies. Because of this gaps in the fossil record are inevitable.

However, new fossils are being found all the time, and many 'transitional' species have been identified that do provide support for evolutionary theory. Take the horse, for instance. Today's horses have one toe, but they evolved from dog-sized ancestors with multi-toed feet. The fossil record shows several intermediate steps, showing how toes were lost, shortened and combined to form the familiar hoof that we see today.



○ Archaeopteryx shows the link between dinosaurs and birds, with key features of both

NATURAL SELECTION DRIVES ALL EVOLUTION

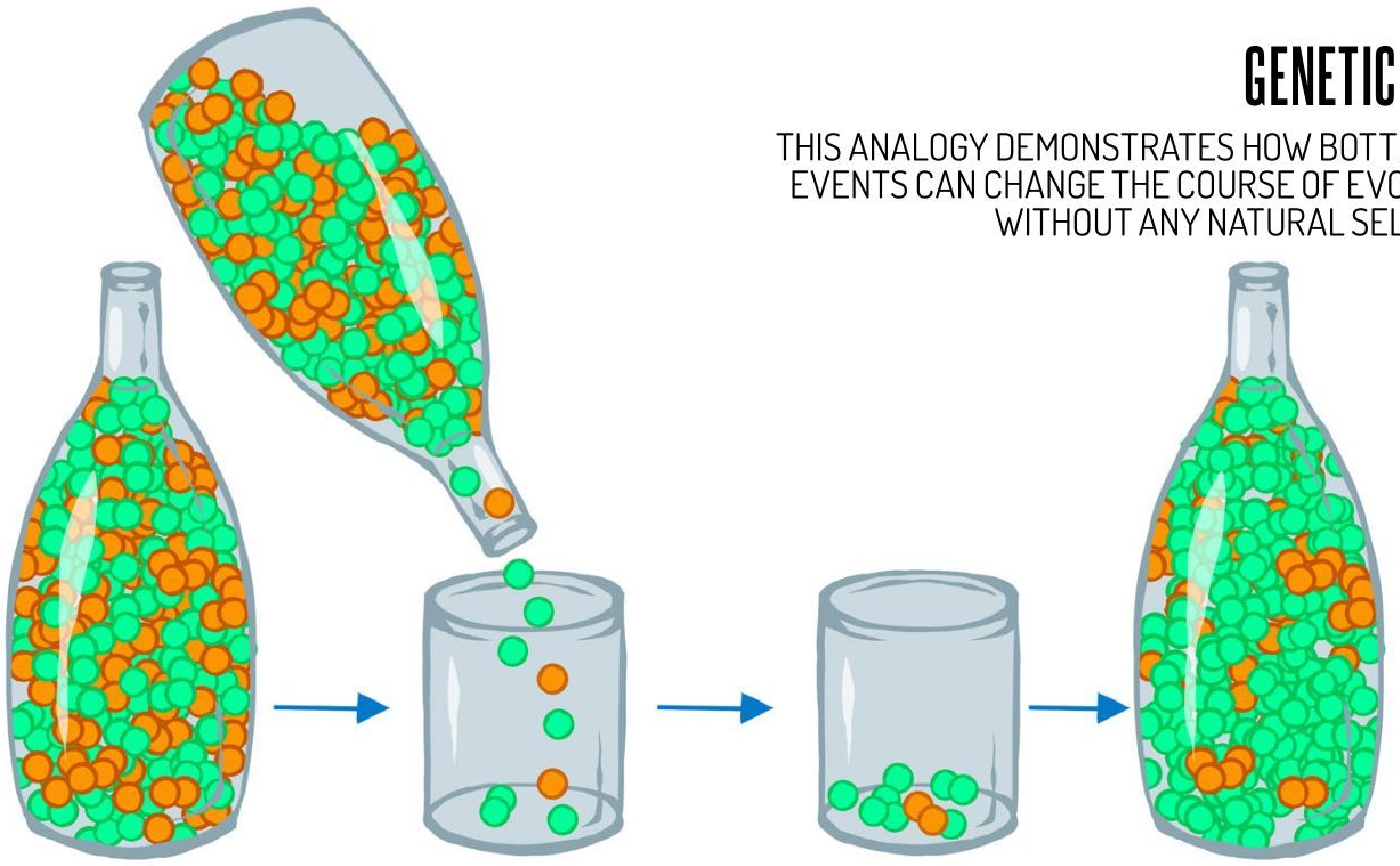
IS SURVIVAL OF THE FITTEST THE ONLY WAY THAT EVOLUTION HAPPENS?

Random mutations of genes can make some individuals slightly different to others, creating genetic variation. Predators, competition and other environmental factors can put pressure on organisms, and those with the most useful adaptations are more likely to survive and breed, passing on their genes to their offspring. This process, called natural selection, is what Darwin is famous for describing, but it isn't the only way that evolution can occur.

Another important mechanism is called genetic drift. Here, rather than traits being selected for, they are lost or become more common due to a random event. This can happen if populations become separated or if some individuals are killed, particularly if the population size is small.

GENETIC DRIFT

THIS ANALOGY DEMONSTRATES HOW BOTTLENECK EVENTS CAN CHANGE THE COURSE OF EVOLUTION WITHOUT ANY NATURAL SELECTION



1. ORIGINAL POPULATION
To start with, this population is mixed, with orange and green individuals in roughly equal proportions.

2. BOTTLENECK
A random event happens, such as a natural disaster, causing the population size to decrease dramatically.

3. REMAINING POPULATION
Now, there are more green individuals than orange; the gene pool has changed by chance.

4. NEW POPULATION
As the remaining population breeds, the genes are passed on, creating a new population where green is much more common. In time, orange could be lost altogether.

EVOLUTION IS 'JUST' A THEORY

WE DON'T KNOW FOR CERTAIN THAT EVOLUTION OCCURS

This one is hard to argue with, given that the word 'theory' is right there in its title, but the real problem is the word 'just'. In science, there's no such thing as 'just' a theory.

In general conversation, the word 'theory' is used interchangeably with words like 'hunch', 'speculation' and 'belief'. It's a fuzzy way to indicate that you think something might be true, but you don't have all of the evidence to back it up. This is not the case in science.

A scientific theory is based on a vast body of evidence. There are many well-established principles of science, including evolution, that are centred around theories – for instance, that Earth orbits the Sun (heliocentric theory) and that living things are made of cells (cell theory). They provide a comprehensive explanation of what we see and can be used to predict what might happen in the future.

The evidence for evolution is compelling, and the theory has been confirmed repeatedly in different ways. The fossil record, though incomplete, demonstrates the progression of organisms over time. This is supported by the physical, chemical and genetic similarities between living things, and there are plenty of real-life examples out there of organisms visibly changing over several generations.

The more evidence scientists find, the more they reinforce Darwin's ideas. Evolution is not 'just' a theory, because in science a theory is one of the strongest and most compelling arguments that can be made.

○ Evidence of evolution is written all over our DNA

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THE SCIENCE OF FEAR

EXPLORE THE BIOLOGY OF BEING AFRAID & WHY THIS
PRIMAL EMOTION IS KEY TO YOUR SURVIVAL

Home alone at night, you hear a loud crash. In an instant your heart starts racing, your muscles tense and your breath quickens. You are immediately alert, primed to fight or flee the source of the sound, which turns out to be a pile of books falling off that shelf you've been meaning to fix. However, in that moment your brain and body instinctively reacted as if you were in mortal danger.

Fear is one of our strongest and most primal emotions. It's a big bad world out there, and being afraid of certain things protects us from potential danger to make sure we survive. Some evolutionary fears are hard-wired into our brains, but we can also develop new fears throughout our lives. As children we pick up on what makes our parents anxious, and we may also learn to fear certain things after negative experiences. Despite this, most of us are able to ignore our fears when it's clear we aren't in any immediate danger. We can enjoy the view from the top of a skyscraper rather than worry about falling, or turn out the lights safe in the knowledge that a predator won't devour us in the night.

However, people with phobias have an excessive fear response that causes both physical and psychological distress. These extreme fears are divided into three different groups: agoraphobia, social phobia and specific phobias. Agoraphobia is generally referred to as the fear of open spaces, but it applies to the dread of any situation that is difficult to escape from or where help would not be available if something went wrong. Social phobia is the intense fear of interacting with people or performing, while specific phobias are the fear of a particular situation, activity or thing.

These irrational fears can cause major disruptions to everyday life; somebody with acrophobia (an extreme fear of heights) may experience a panic attack simply trying to walk across a bridge. Depending on the trigger of their phobia, sufferers often go to great lengths to avoid situations that could affect them.

The cause of phobias is not always clear, but many cases are linked to experiencing or witnessing a traumatic event. For example, somebody may develop cynophobia (the fear of dogs) after being bitten. But whether the trigger is rational or irrational, as soon as the brain registers a scary stimulus it activates the fight-or-flight response, thus preparing the body for action.

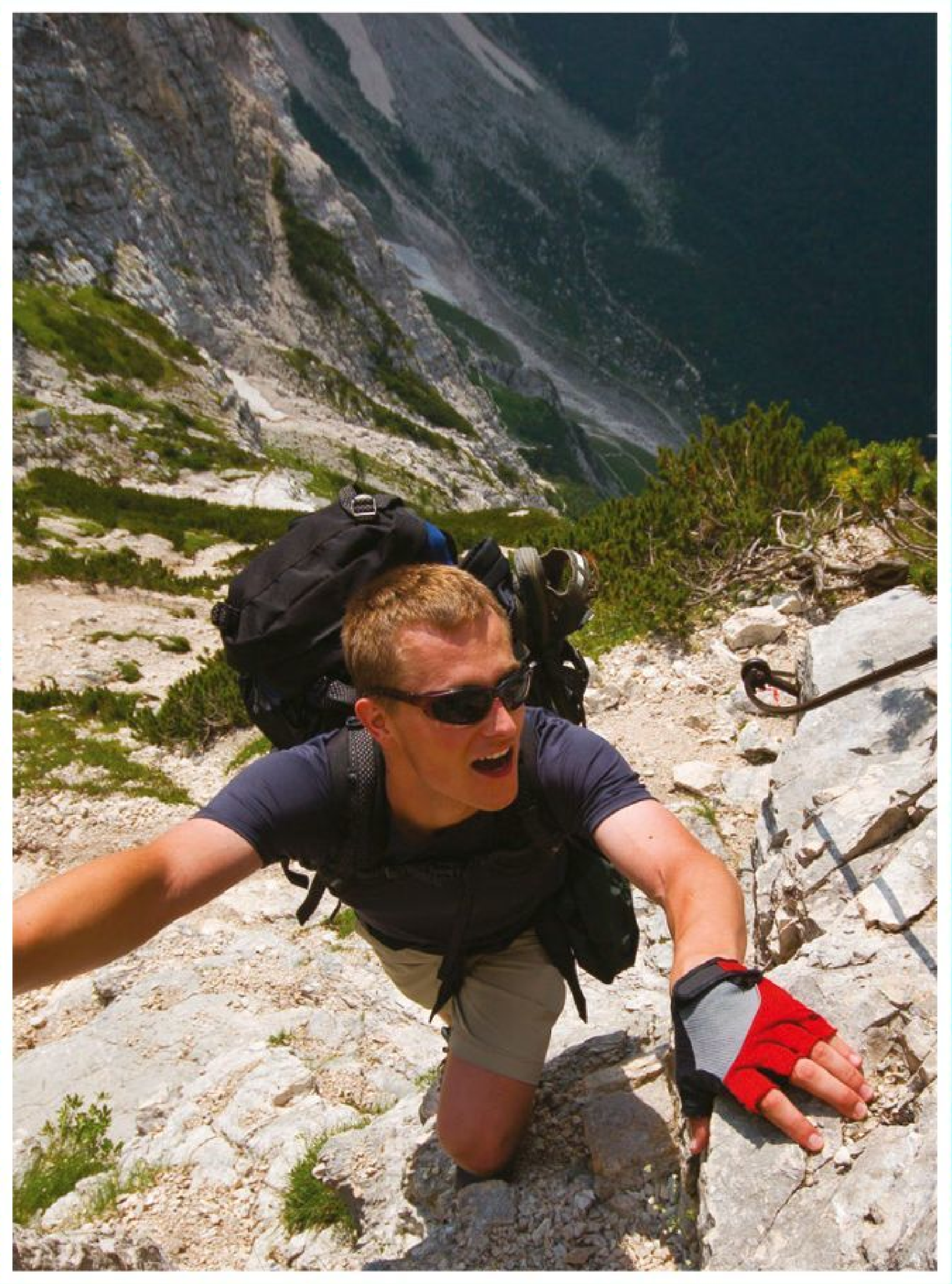
NATURAL FEARS

SOME OF OUR FEARS HAVE DEVELOPED AS AN EVOLUTIONARY RESPONSE TO DANGER

> "Even today, the majority of African lion attacks on humans occur after dark"

DARKNESS

Sight is arguably our most important sense. When we are faced with pitch-darkness we are left vulnerable, unaware of what is around us. At night our early ancestors were at risk of being attacked by nocturnal predators. A study from 2011 found that even today, the majority of African lion attacks on humans occur after dark and are more likely when the Moon is below the horizon. Although being hunted while we sleep isn't a risk for most of us, we are instinctively more anxious when unable to see.



HEIGHTS

A fear of heights is necessary to our survival, ensuring we are cautious in situations where we might injure ourselves. To study this, researchers set up a platform surrounded by a transparent material, giving the illusion of a cliff, and put young children on the platform to test their reaction. They found that most infants didn't try to move onto the transparent section, suggesting that they inherently avoided risking a drop. As our ancestors explored the world, this fear ensured they were wary of climbing to dangerous heights.

VENOMOUS CREATURES

While we may not be terrified of them from birth, evidence suggests that we are predisposed to detect and recognise spiders and snakes quicker than non-threatening animals. One theory is that our early mammal ancestors, evolving in a world dominated by reptiles, needed to identify and react to snakes to avoid becoming dinner. Another hypothesis is that our ancestors evolving in Africa coexisted with a number of venomous spider species for millions of years, so being able to spot and avoid them was a vital skill.

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FIGHT OR FLIGHT

HOW YOUR BRAIN AND BODY TRIGGER THIS EVOLUTIONARY SURVIVAL INSTINCT

○ A fear of flying is relatively common and may have roots in the evolutionary fear of heights

Under normal circumstances, sensory information from your body is sent to the thalamus in the brain. The thalamus relays these signals to the cortex and the hippocampus for further processing to provide a better understanding of what you're experiencing and put it into context. This analysis is forwarded to the amygdala, which triggers an appropriate emotional reaction to the situation.

When your brain receives signals that indicate some kind of danger, the course of action is slightly different. The process above still occurs, but this higher-level analysis takes precious time. The fraction of a second it takes to fully understand what's happening might be the difference between life and death. To make sure your body is instantly prepared to face a threat, the thalamus also sends the raw sensory information directly to the amygdala via a shortcut.

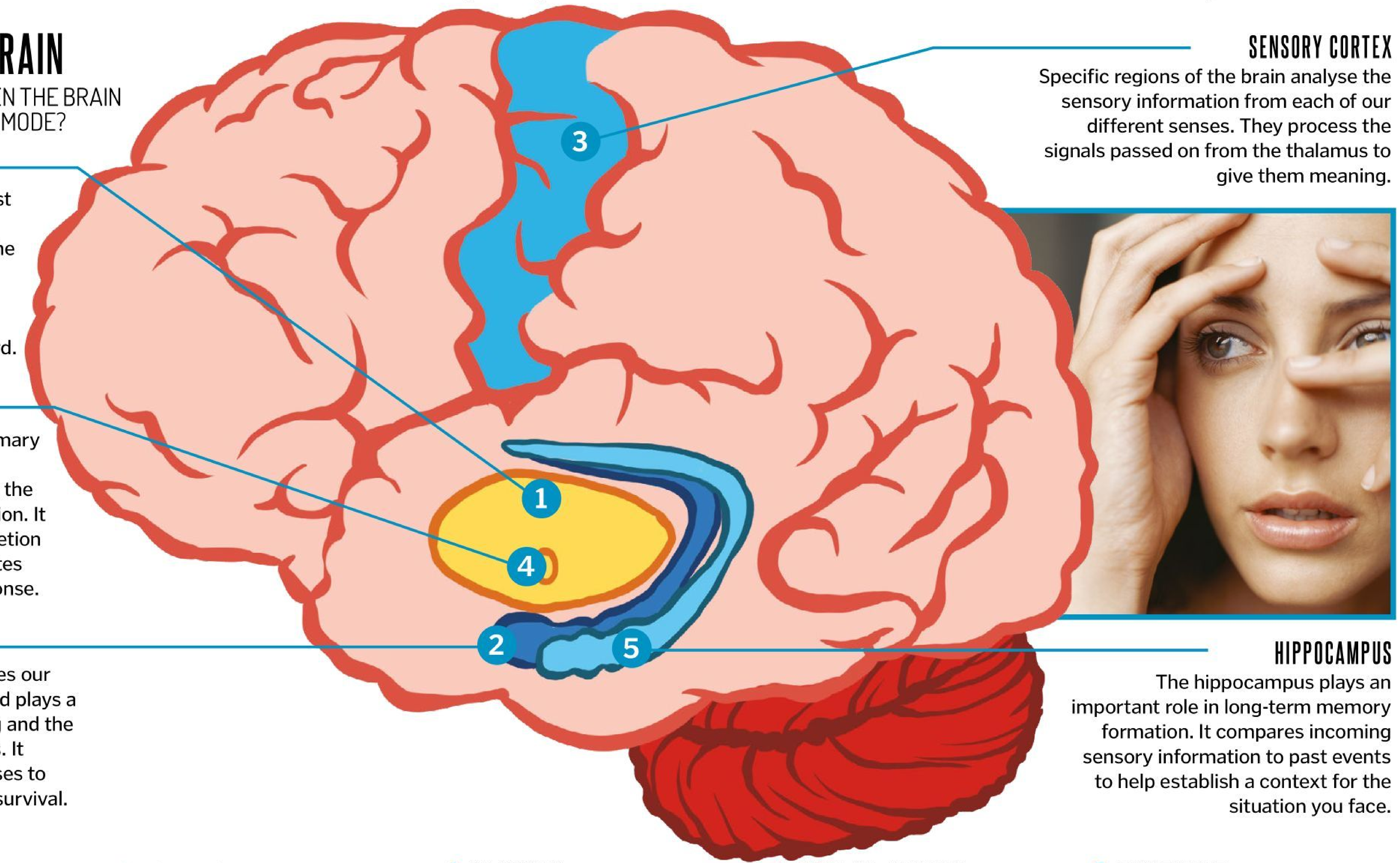
As soon as the amygdala is alerted it signals the hypothalamus. This part of the brain activates systems that release a cocktail of around 30 different hormones into the bloodstream. One hormone in particular, adrenaline, causes a variety of physiological reactions all around the body. For example, in the lungs it makes smooth muscle cells relax, expanding the air passages so more oxygen can reach the blood. It also stimulates cardiac cells so the heart beats faster and makes muscles in the eyes contract to dilate the pupils. The physical changes produced by this sudden flood of hormones make up what is known as the fight-or-flight response. This instinctive reaction gets you ready to either take a stand and defend yourself or escape to safety.

Not many of us experience life-threatening situations day-to-day, so more often than not our fight-or-flight response is triggered by a false alarm. The moment of panic you feel after hearing a loud bang, for example, is because neural signals from the shortcut reach the amygdala first. The fight-or-flight response automatically kicks in before the brain evaluates the situation, just in case. Once the amygdala receives more information and concludes you aren't in danger it signals the thalamus to stop the fight-or-flight reaction, returning your body to normal.

The human brain is hard-wired to prepare for the worst; it may seem silly to treat every loud noise as a danger, but if the threat turns out to be real this overreaction could save your life.

FEAR ON THE BRAIN

WHAT HAPPENS WHEN THE BRAIN GOES INTO SURVIVAL MODE?



THALAMUS
The thalamus is the first port of call for most sensory signals from the body. It relays this information to the relevant areas of the brain, like a switchboard.

HYPOTHALAMUS
The hypothalamus' primary role is to maintain homeostasis – keeping the body in a stable condition. It also regulates the secretion of hormones and initiates the fight-or-flight response.

AMYGDALA
The amygdala processes our emotional reactions and plays a role in decision-making and the formation of memories. It moderates our responses to events that affect our survival.

SENSORY CORTEX
Specific regions of the brain analyse the sensory information from each of our different senses. They process the signals passed on from the thalamus to give them meaning.

HIPPOCAMPUS
The hippocampus plays an important role in long-term memory formation. It compares incoming sensory information to past events to help establish a context for the situation you face.

1 STIMULUS

When a potential threat is detected, the thalamus sends signals to the amygdala via two different pathways. One route is fast and direct, while the slower path analyses the situation and decides what should happen next.

2 ACT FIRST

The first pathway immediately assumes there's danger even if there is none – a safer option than vice versa. It goes directly to the amygdala, which sends signals to the hypothalamus to initiate the fight-or-flight response.

3 ANALYSIS

The same information is sent along the more investigative route. Signals from the thalamus are sent to the sensory cortex, which interprets the data, followed by the hippocampus, to analyse the context of the situation.

4 FIGHT OR FLIGHT?

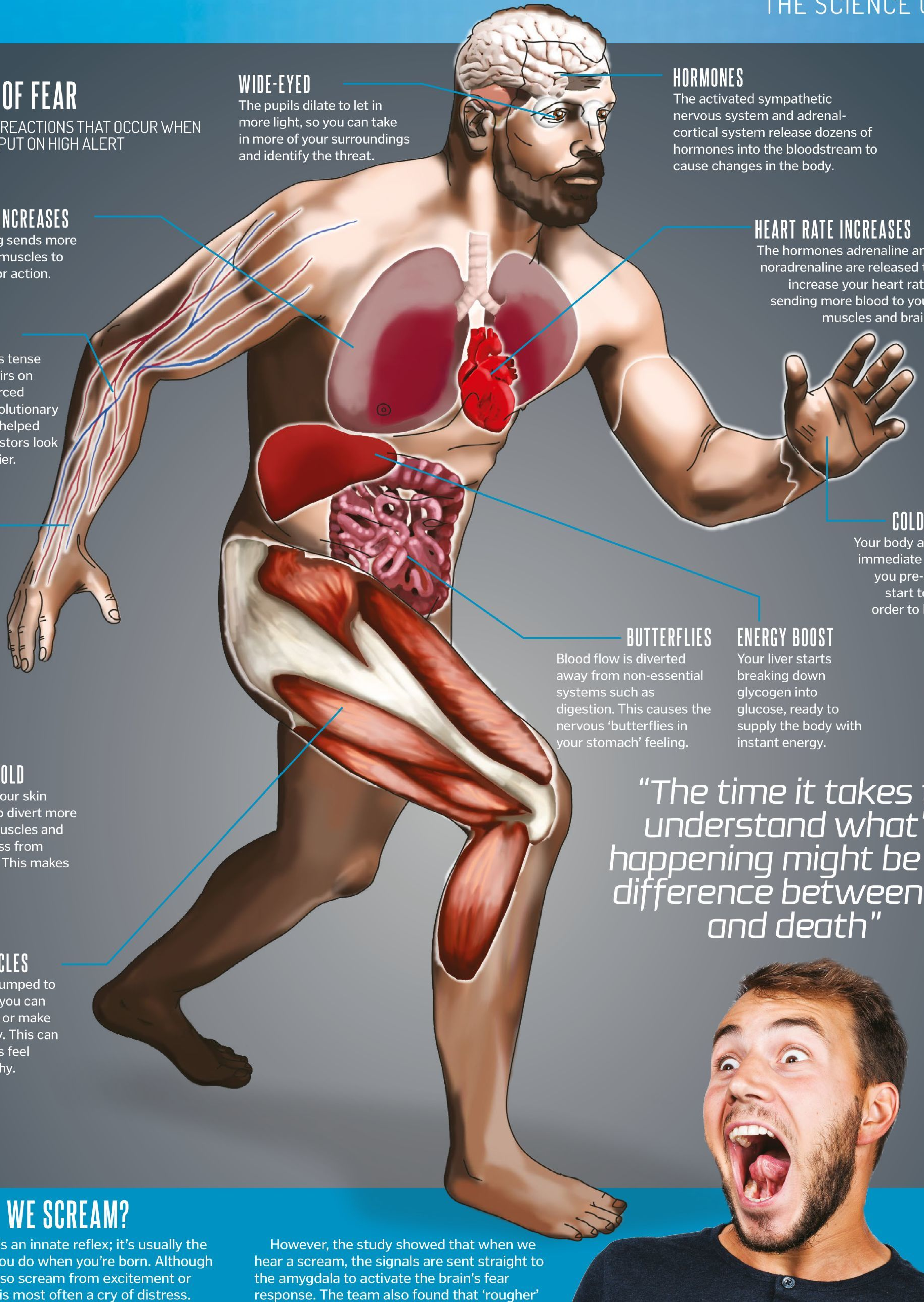
The hypothalamus activates both the sympathetic nervous system and the adrenal-cortical system to trigger the fight-or-flight reaction. The impulses and hormones produced prepare the body for action.

5 JUDGEMENT

Once the situation has been analysed by the longer pathway, the hippocampus sends signals to the amygdala to either seize the fight-or-flight response if there is no danger or to maintain it if there is.

ANATOMY OF FEAR

THE EXTREME REACTIONS THAT OCCUR WHEN YOUR BODY IS PUT ON HIGH ALERT



WIDE-EYED

The pupils dilate to let in more light, so you can take in more of your surroundings and identify the threat.

HORMONES

The activated sympathetic nervous system and adrenal-cortical system release dozens of hormones into the bloodstream to cause changes in the body.

RESPIRATION INCREASES

Faster breathing sends more oxygen to your muscles to prepare them for action.

HEART RATE INCREASES

The hormones adrenaline and noradrenaline are released to increase your heart rate, sending more blood to your muscles and brain.

GOOSEBUMPS

As your muscles tense up, the small hairs on your skin are forced upright. This evolutionary reflex probably helped our hairier ancestors look bigger and scarier.

COLD SWEAT

Your body anticipates immediate action, so you pre-emptively start to sweat in order to keep cool.

BUTTERFLIES

Blood flow is diverted away from non-essential systems such as digestion. This causes the nervous 'butterflies in your stomach' feeling.

ENERGY BOOST

Your liver starts breaking down glycogen into glucose, ready to supply the body with instant energy.

BLOOD RUNS COLD

The vessels in your skin constrict to help divert more blood to your muscles and reduce blood loss from potential injury. This makes you feel cold.

SHAKING MUSCLES

More blood is pumped to the muscles so you can defend yourself or make a quick getaway. This can make your limbs feel tense and twitchy.

> *"The time it takes to understand what's happening might be the difference between life and death"*

WHY DO WE SCREAM?

Screaming is an innate reflex; it's usually the first thing you do when you're born. Although we might also scream from excitement or pleasure, it is most often a cry of distress. Researchers from New York University conducted an experiment using brain scans to see how our minds react to screams. When we listen to normal speech, what we hear is sent to the auditory cortex for processing so we can make sense of the sounds.

However, the study showed that when we hear a scream, the signals are sent straight to the amygdala to activate the brain's fear response. The team also found that 'rougher' screams – those that change volume more quickly – were the most distressing. The results show that screams are a very effective method of communication in humans. They not only help convey danger but also help make those who hear them more alert.

○ Screams are an example of a universal vocalisation; they are the same in every language

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ARE FEARS GENETIC?

YOUR PHOBIAS COULD BE PASSED DOWN THROUGH GENERATIONS IN DNA

It was previously assumed that all irrational fears are learned through personal experience or taught to us by others. In cases where a person develops a phobia related to a traumatic event in their past, this is most likely the case. If somebody nearly drowns while swimming in the sea, for instance, it wouldn't be surprising if they develop aquaphobia (the fear of water). The brain makes a connection between the situation and the feeling of pain and panic and commits it to memory.

However, it is now thought that some phobias have a genetic origin. Identical twins are more likely to share the same irrational fears than non-identical twins, even if they are raised apart from one another.

Experiments with mice have shown that fears they develop can be passed down to their children and even their grandchildren. The mice were conditioned to fear the scent of acetophenone – a sweet-smelling chemical. Researchers found that the pups, and even the grand-pups, of the conditioned mice were startled by the scent too.

One explanation for this could be that parent mice communicate with their pups to effectively teach them what to fear. Studies have found that when mice are scared they release pheromones that act as an alarm signal to other mice. However, in the acetophenone experiment the pups proved to be sensitive to the scent from the very first time they encountered it. What's more, some pups of conditioned mice were fostered by non-conditioned mice. The non-conditioned foster parents were not afraid of the scent but the pups were, suggesting the fear's origin was genetic rather than social.

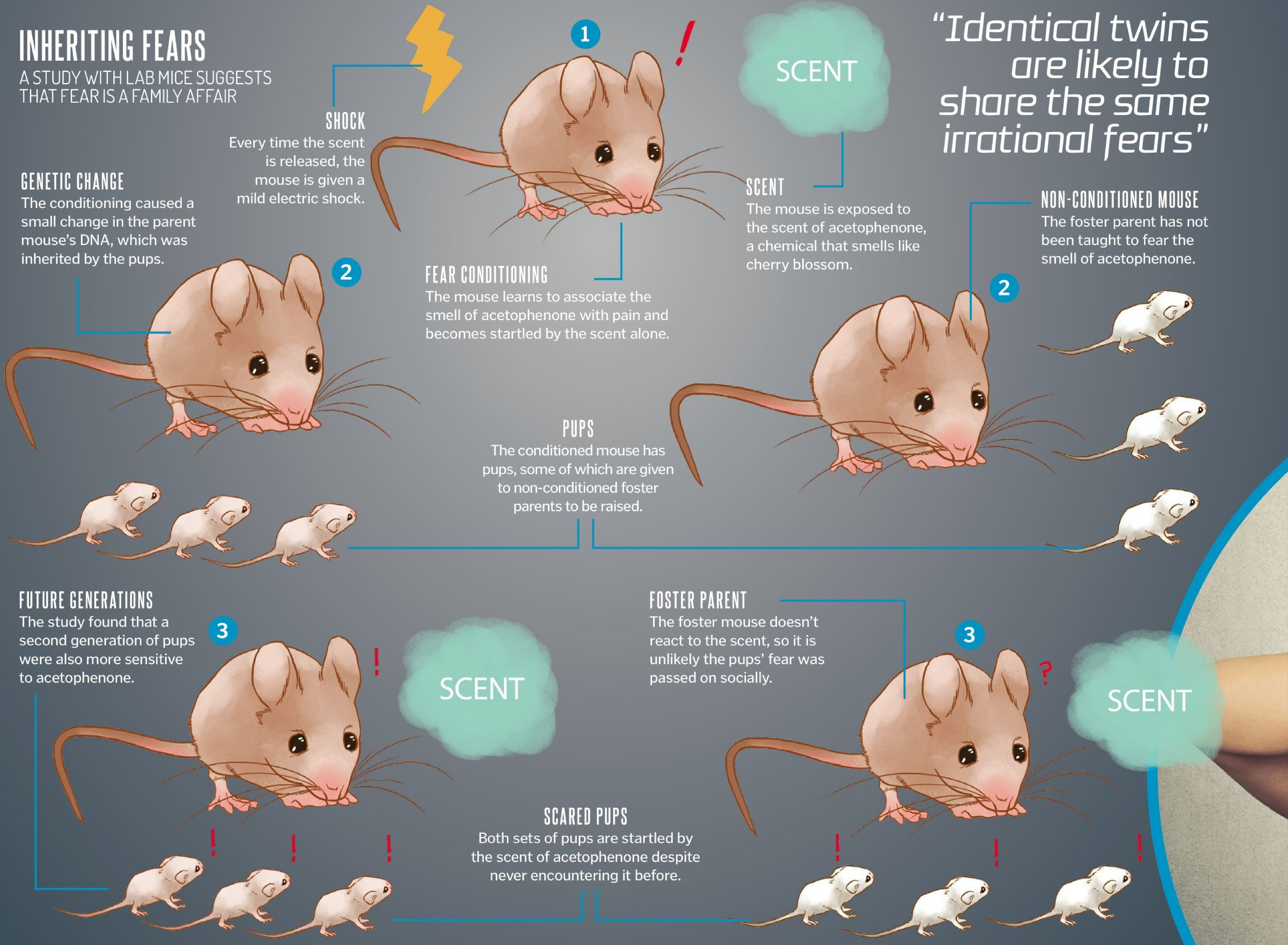
It is not clear exactly how the conditioned fear is passed on to future generations of mice, but the current theory is that it is down to something called epigenetic inheritance. The original conditioning process leads to chemical modifications that change gene expression (which genes are switched on or off) without changing the DNA sequence itself. The researchers found that the conditioned mice and their offspring developed more scent receptors in their brains compared to non-conditioned mice. With more of these receptors they can detect the presence of acetophenone at lower concentrations and so are alerted to it more easily.

Epigenetics is a relatively new area of research, but it stands to reason that fears and other memories may well be inherited this way in humans too.

> *"Identical twins are likely to share the same irrational fears"*

INHERITING FEARS

A STUDY WITH LAB MICE SUGGESTS THAT FEAR IS A FAMILY AFFAIR



SHOCK
Every time the scent is released, the mouse is given a mild electric shock.

SCENT
The mouse is exposed to the scent of acetophenone, a chemical that smells like cherry blossom.

FEAR CONDITIONING
The mouse learns to associate the smell of acetophenone with pain and becomes startled by the scent alone.

GENETIC CHANGE
The conditioning caused a small change in the parent mouse's DNA, which was inherited by the pups.

NON-CONDITIONED MOUSE
The foster parent has not been taught to fear the smell of acetophenone.

PUPS
The conditioned mouse has pups, some of which are given to non-conditioned foster parents to be raised.

FUTURE GENERATIONS
The study found that a second generation of pups were also more sensitive to acetophenone.

FOSTER PARENT
The foster mouse doesn't react to the scent, so it is unlikely the pups' fear was passed on socially.

SCARED PUPS
Both sets of pups are startled by the scent of acetophenone despite never encountering it before.

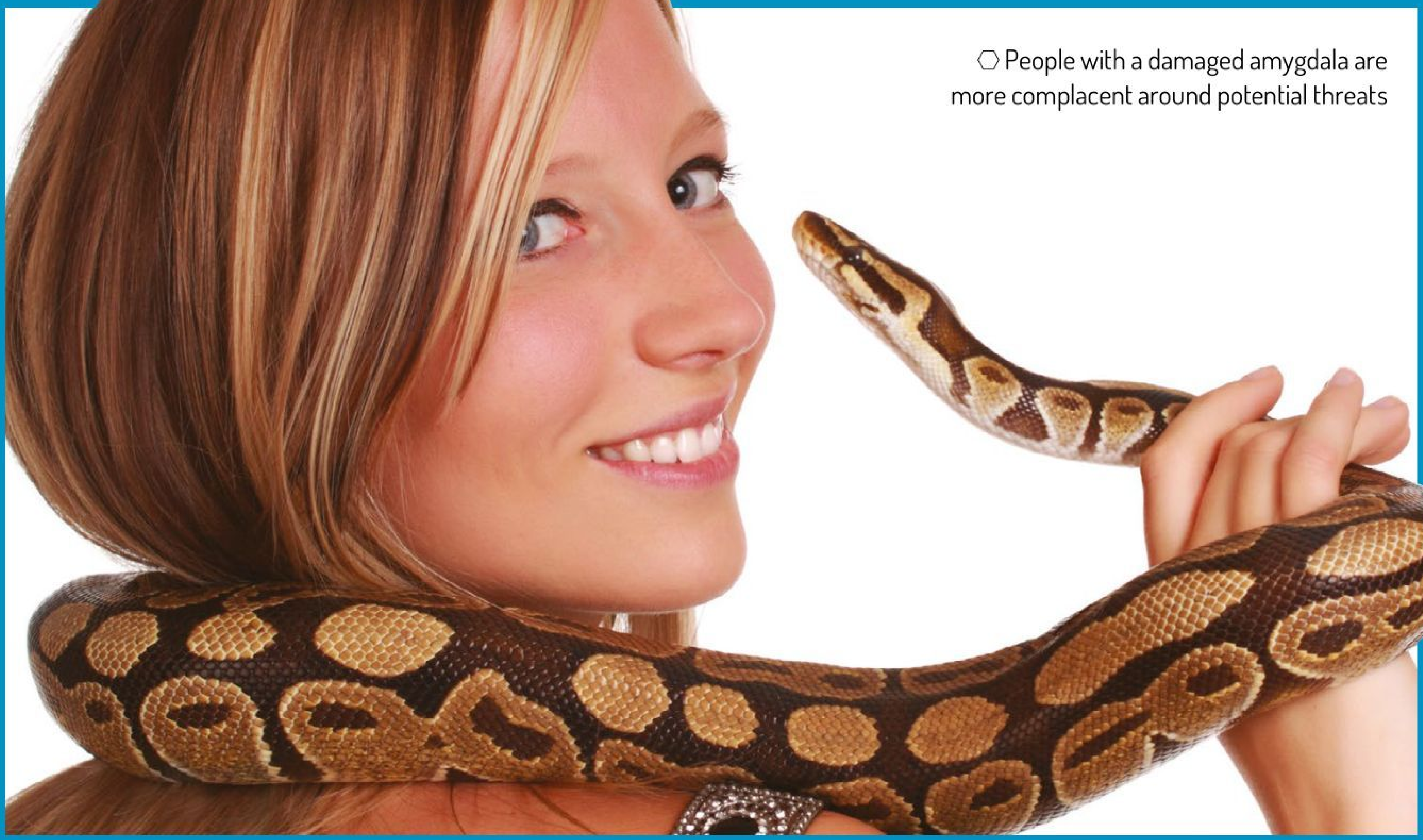
LIVING FEARLESSLY

Self-help gurus and motivational posters encourage us to be fearless, but in reality a life without fear would be incredibly dangerous. Studies have shown that when the region of the brain called the amygdala is damaged people are more likely to take risks. Severe damage can even leave people with no sense of fear whatsoever – which can land them in some pretty scary situations!

For the past 25 years scientists have been studying a patient (known as SM for anonymity) who lacks an amygdala. SM has experienced many traumatic events in her life – she has been held at both knife- and gun-point, and was nearly killed during a domestic violence attack – but she did not react with any sense of desperation or urgency, even though her life was in danger.

Researchers took SM to an exotic pet store where, despite claiming she hated them, the snakes and spiders captivated her. Scientists noted her curiosity and compulsive desire to touch some of the more dangerous creatures, following repeated warnings from staff. The researchers concluded that SM's inability to detect or react appropriately to threats likely contributed to her disproportionate number of traumatic experiences.

By studying patients like SM, it is hoped that scientists can understand more about fear and discover new methods of helping people whose lives are plagued by it. For example, treatments that target the amygdala could benefit those who suffer from post-traumatic stress disorder.



People with a damaged amygdala are more complacent around potential threats

Sometimes it is just the thrill that makes people take unnecessary risks

Regularly activating the fight-or-flight response through anxiety or stress can cause serious health problems

SCARED TO DEATH

It's not just a figure of speech – it turns out you really can die of fright. The adrenaline released during the fight-or-flight response can be damaging in large amounts. This stress hormone encourages the heart muscle to contract, but if your body releases too much adrenaline your heart is unable to relax again. Adrenaline can also interfere with the cells that regulate your heart rhythm, causing it to beat abnormally, which could be lethal.

While not directly deadly, prolonged anxiety can have a significant negative impact on your health. The fight-or-flight response suppresses the immune system, leaving you vulnerable to illness. Going into survival mode on a regular basis can lead to digestive disorders as this non-essential system is repressed. Long-term stress can also lead to weight issues by disrupting the metabolism; elevated levels of cortisol can make the body less sensitive to insulin. Muscles that are constantly tense and ready for action can cause headaches, stiffness and neck pain. The list doesn't end there; chronic anxiety has also been linked to cardiovascular problems, asthma and insomnia. Such a broad range of effects can be harmful to both physical and mental wellbeing.

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Fear is an instinctive survival mechanism that helps protect us from danger

FACING YOUR FEARS

CAN YOU RETRAIN YOUR BRAIN TO OVERCOME A PHOBIA?

Some phobia triggers are much easier to avoid than others. For example, people who suffer from a fear of bats (chiroptophobia) are highly unlikely to be plagued by these creatures day in, day out. Someone suffering from a social phobia, however, will struggle to lead a normal life.

There are a variety of different methods used to treat phobias. Among the most popular are talking treatments, such as cognitive behavioural therapy and exposure therapy, which work by retraining the brain to change how it responds to a phobia trigger. The approach is essentially the opposite of fear conditioning – the patient learns to associate their trigger with more rational, positive thoughts.

Another approach being investigated is tricking the brain into treating itself. Mentalist and illusionist Derren Brown conducted an experiment on his programme *Fear and Faith* in which he gave people with different phobias a new wonder drug called Rumyodin. One subject, usually terrified of heights, was comfortably able to sit on the edge of a tall bridge. Another volunteer with a fear of performing in public was able to go to an audition. It was revealed that Rumyodin (an anagram of 'your mind') didn't exist, and the participants had simply been injected with saline solution and given sugar pills.

The incredible results are a demonstration of the placebo effect, a phenomenon in which a fake treatment has a very real result. Scientists are investigating how this effect can be exploited to treat both physical and psychological problems.

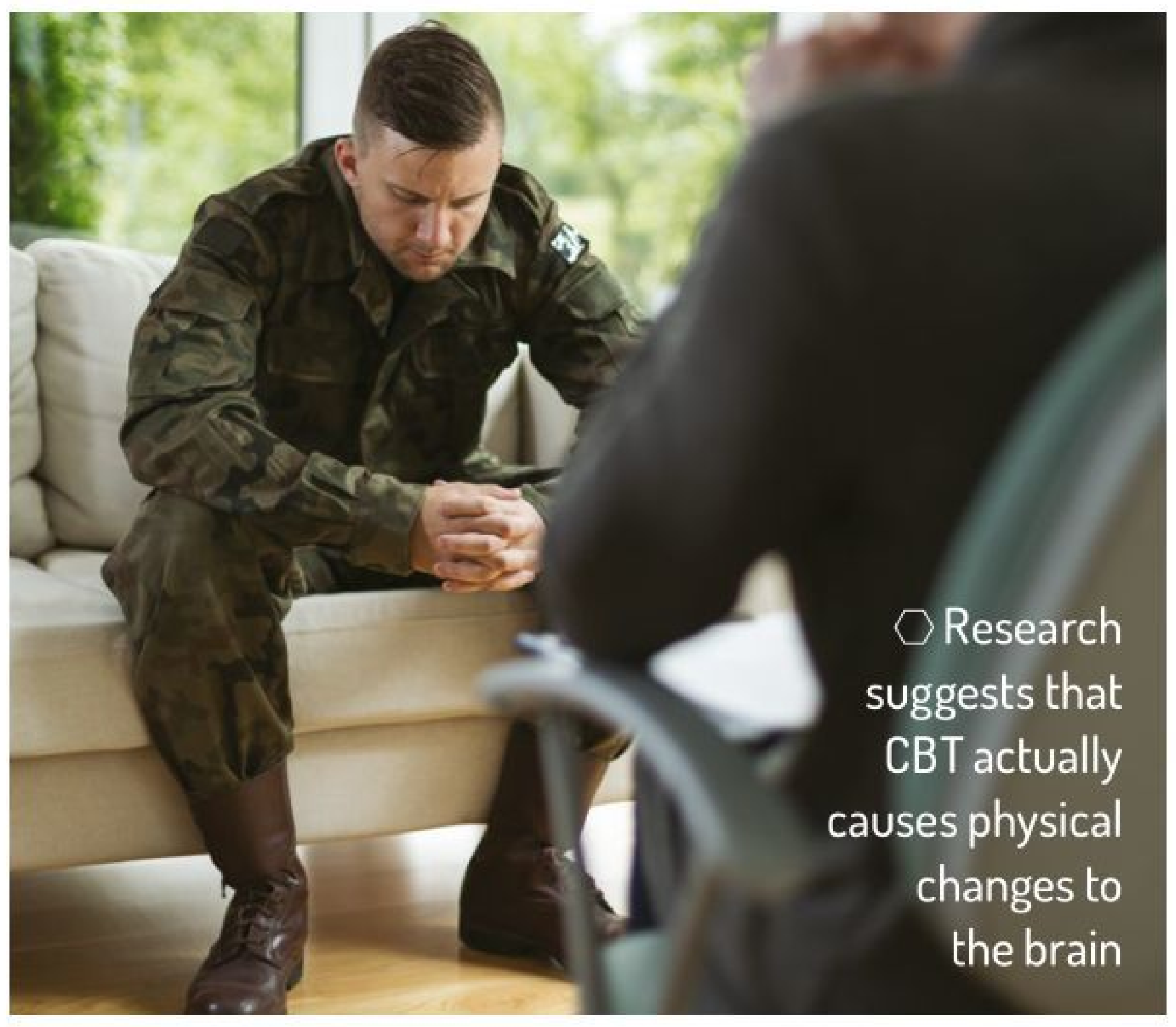
PHOBIA TREATMENTS

Exposure therapy involves facing your fears one step at a time

> *"The patient learns to associate their phobia trigger with more rational, positive thoughts"*

EXPOSURE THERAPY

The aim of exposure therapy is to gradually desensitise the patient to the source of their phobia. The patient ranks situations from least to most terrifying. For example, an arachnophobe might place thinking about a spider at the bottom of their list and having a spider crawl along their arm at the top. The patient works with a psychologist to systematically work their way through the list, using relaxation techniques or other coping mechanisms until they are comfortable with each stage. The patient's brain learns to relate each scary situation to being calm, reducing their anxiety.



Research suggests that CBT actually causes physical changes to the brain

COGNITIVE BEHAVIOURAL THERAPY

The aim of cognitive behavioural therapy (CBT) is to change how we think about certain situations. It is thought that irrational anxiety issues are caused by a patient's negative interpretation of events rather than the events themselves. CBT is a talking therapy that helps patients assess their reactions to situations, replacing the worry cycle with more useful or realistic thoughts. Patients' brain scans indicate that CBT reduces the overactivity in the amygdala and hippocampus associated with phobias. Studies have also shown that CBT is as effective as medication in the treatment of many anxiety disorders.

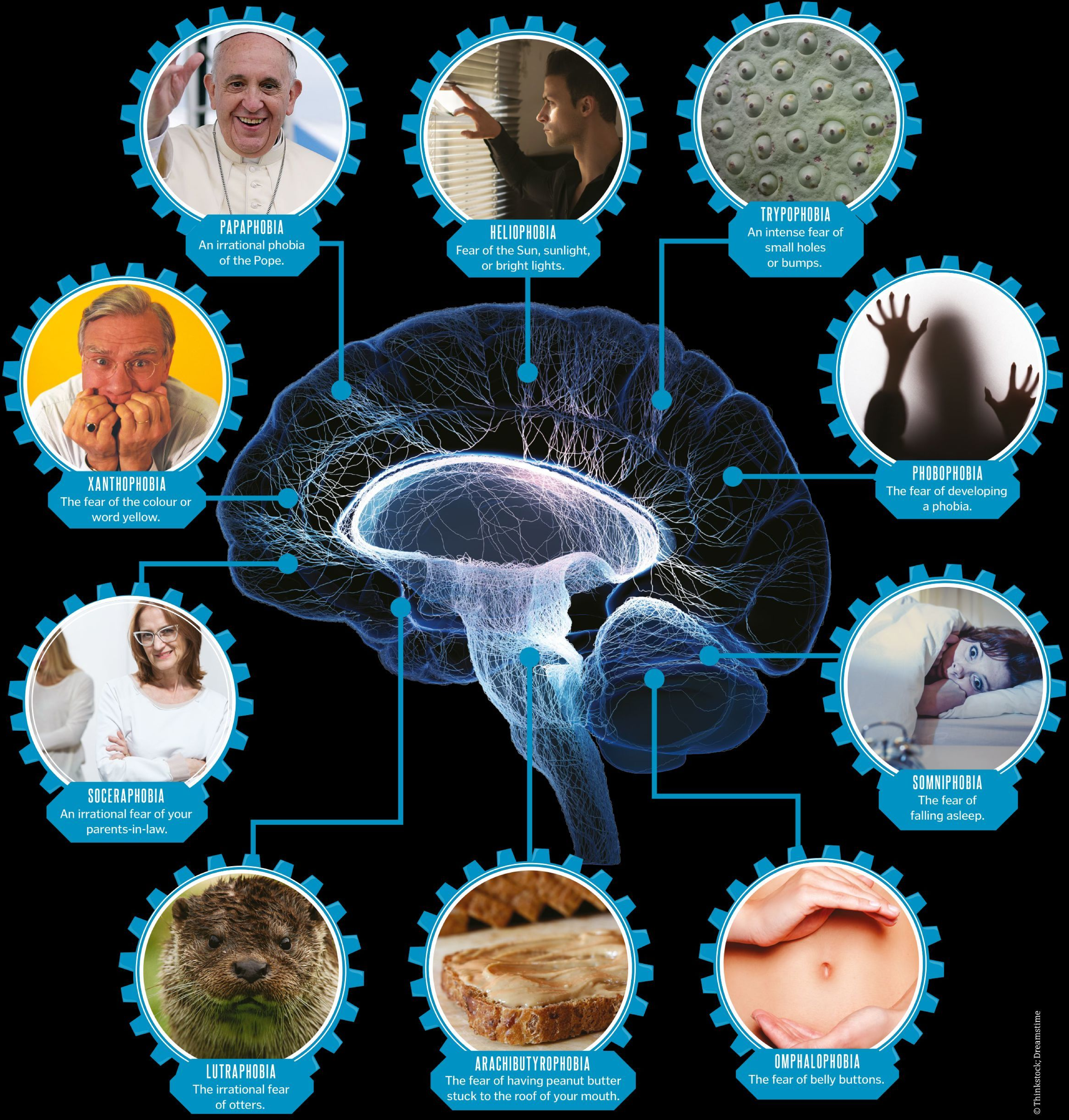
Therapists can control the virtual scenario to suit the patient's progress

VIRTUAL REALITY THERAPY

Exposure therapy isn't a viable option for all phobias, but modern technology offers an alternative. Advancements in virtual reality systems mean that patients can now face their fears through a headset rather than in the real world. This allows patients to face any number of situations relating to their phobia while knowing they are in no physical danger. For example, somebody with a phobia of flying can take a course of sessions in which they board a virtual plane and experience announcements, take-off, turbulence and landing without having to buy a plane ticket each week.

TOP 10 STRANGEST PHOBIAS

THE MOST COMMON PHOBIAS STEM FROM RATIONAL FEARS, BUT OTHERS ARE COMPLETELY BIZARRE



PAPAPHOBIA
An irrational phobia of the Pope.

HELIOPHOBIA
Fear of the Sun, sunlight, or bright lights.

TRYPOPHOBIA
An intense fear of small holes or bumps.

XANTHOPHOBIA
The fear of the colour or word yellow.

PHOBOPHOBIA
The fear of developing a phobia.

SOCERAPHOBIA
An irrational fear of your parents-in-law.

SOMNIPHOBIA
The fear of falling asleep.

LUTRAPHOBIA
The irrational fear of otters.

ARACHIBUTYROPHOBIA
The fear of having peanut butter stuck to the roof of your mouth.

OMPHALOPHOBIA
The fear of belly buttons.

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YOUR FIRST YEAR

WHAT HAPPENS TO THE HUMAN BODY IN THE FIRST 12 MONTHS OF LIFE

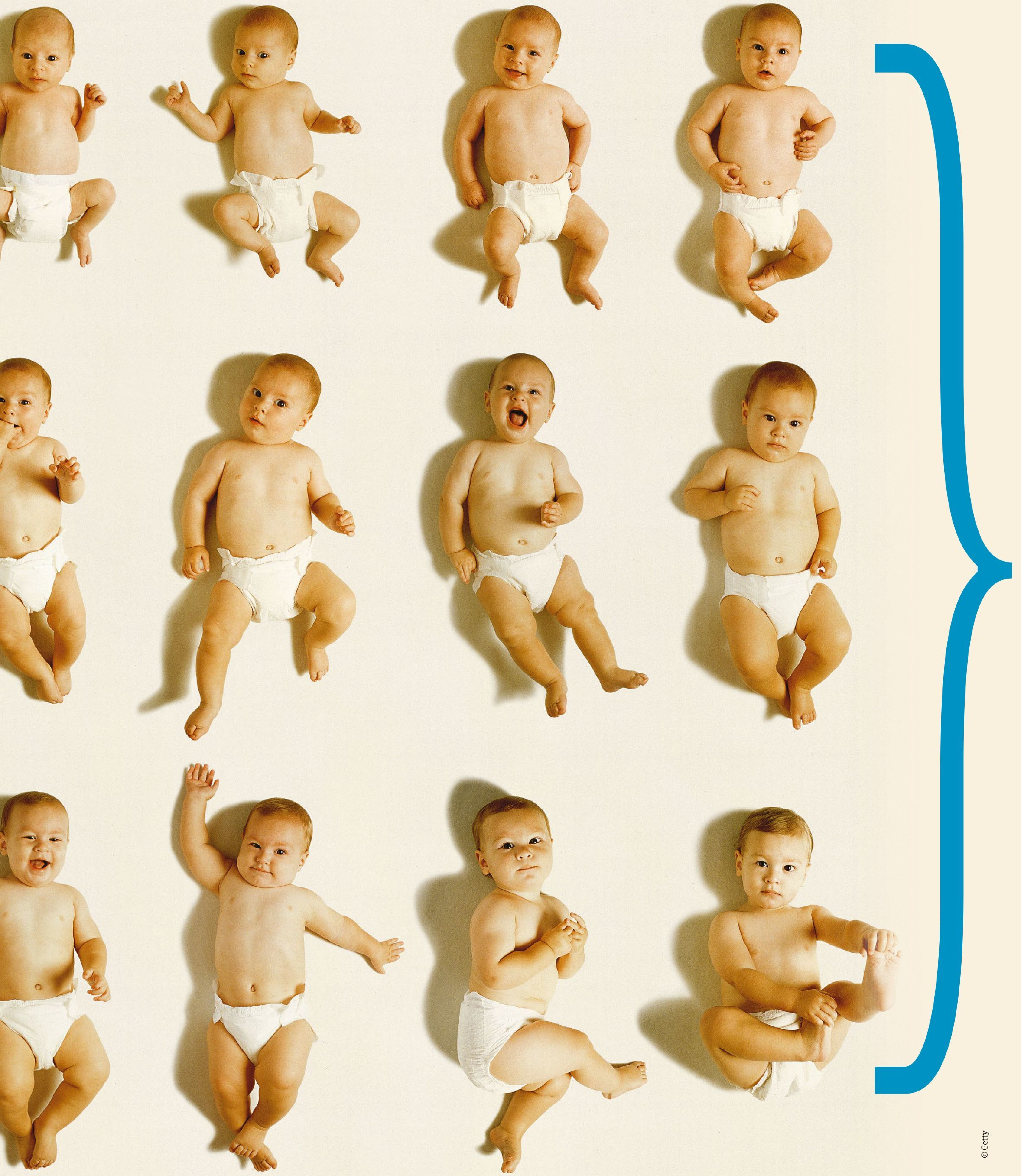
We are born well before we're ready to fend for ourselves, but we learn faster in our first three years than we will for the rest of our lives. So how do we get from vulnerable newborns unable to lift our own heads to walking, talking toddlers?

BIRTH

Babies enter the world with a lot of growing left to do. From around 35 weeks of pregnancy babies start becoming cramped. As the foetus gets bigger it demands more and more energy, and there's only so much that the mother can supply. Before they are born, their growth starts to slow.

Entering the world for the first time is a shock to a baby's system, and the first days of life are critical. Until the moment they emerge from the womb, their mother's body has supported every one of their needs. She maintains a constant temperature, digests food to supply nutrients and breathes to supply oxygen. She also deals with waste and fends off infection. Then suddenly the baby has to fend for itself.

As it hits the cold air of the delivery room, a powerful inward breath pulls its lungs open and fills them with air. In the safety of the womb, all the oxygen the baby needed came from the umbilical cord. The lungs were full of amniotic fluid and the heart diverted blood past them through a hole called the foramen ovale and a tube called the ductus arteriosus. Suddenly the baby needs to breathe. The hole in the heart slams shut and blood rushes into the lungs. Within hours or days after birth the tube, and another that carried blood from the umbilical cord to the heart (ductus venosus), closes too.



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WHAT IS
AVAXHOME?

AVAXHOME -

the biggest Internet portal, providing you various content: brand new books, trending movies, fresh magazines, hot games, recent software, latest music releases.

Unlimited satisfaction one low price
Cheap constant access to piping hot media
Protect your downloadings from Big brother
Safer, than torrent-trackers

18 years of seamless operation and our users' satisfaction

All languages
Brand new content
One site

AVXLIVE.ICU

AvaxHome - Your End Place

We have everything for all of your needs. Just open https://avxlive.icu

The other organ systems also spring into action. The baby has been practising breathing and swallowing in the womb, and the kidneys have already started working. Within 24 hours the gut starts moving, passing a dark green or black, tarry substance called meconium. It contains bile, mucus, amniotic fluid and anything else the baby has ingested in utero. Once this fluid is out of the way milk digestion can begin.

The newborn stomach is tiny – barely the size of a marble – so the baby needs to wake every few hours to feed. It can only take a few small mouthfuls at a time. The mother produces a thick, golden-yellow breast milk called colostrum. It's packed with energy but is lower in fat than normal breast milk, which newborns can find hard to digest. Instead, it's full of protein – perfect for a growing baby.

"Babies are born with vital reflexes built in"

Colostrum has a mild laxative effect, which helps to get the baby's gut moving, and it comes with a secret weapon: antibodies. These neutralise bacteria and viruses, sticking them together and triggering their destruction. Throughout pregnancy they cross from mother to baby via the placenta, but this type of immunity is only temporary. The baby will be able to make its own, but this takes a few months. In the meantime, colostrum provides a boost, helping to stave off infection.

The newborn has some tricks of its own to help it survive this vulnerable time. Though they have a lot to learn, babies are born with some vital reflexes built in. These include simple things like blinking, swallowing and yawning, along with more complicated responses.

The rooting reflex makes the baby turn their head or open their mouth when something touches their cheek or lip, and the suck reflex makes them suck if something touches the roof of their mouth. These instincts help with feeding.

Then there are the Moro reflex and the palmar grasp reflex. The first happens when a baby feels as if they are falling. They extend their arms and legs and arch their backs before curling up. The second makes the fingers and toes curl if you touch the palm of their hand or the soles of their feet. Together they help the baby to survive.

FIRST WEEKS

Brand-new babies can hear and respond to noises and are born with the beginnings of communication. They will turn their head towards light and sound, make out the face of the person holding them and cry when they are in need. It only takes a few weeks for these skills to start to improve. They rapidly start to recognise the voice of their mother, and soon they begin to make different noises, cooing and gurgling as well as crying.

For the first few weeks babies can only focus on objects right in front of their faces, and their eyes frequently cross. At this stage their hand-eye coordination is poor. Very young babies will investigate their own hands and fingers, but they can't yet use them properly, and they often keep their hands in fists.

Inside, their bodies are undergoing rapid change fuelled by milk. If the baby is being breastfed, normal breast milk has now replaced colostrum. It's higher in fat and contains enzymes that help the digestive system to access the nutrients. It's also packed with sugars. Not only do these provide energy, they also help friendly bacteria to colonise the large intestine.

Babies are ready to try their first meal at around six months old

WHY DO BABIES SLEEP SO MUCH?

Brand new infants spend around 16 hours a day in the land of nod. At first they wake often to feed, but by the time they are 12 weeks old and weigh on average 5.7 kilograms they begin to sleep for longer periods.

Like adults, babies cycle through four sleep stages. They begin with the lightest dozing before a gradual drop into the deepest slumber, and this rhythm starts when they are still in the womb. Between these cycles they go through phases of rapid eye movement (REM) sleep, spending up to half of their sleep time dreaming.

Early work suggests that sleep is important for consolidating learning and for brain plasticity. In other words, it helps with the strengthening and pruning of connections between different nerve pathways in the brain. Some studies suggest that inadequate sleep may cause problems in the refinement of nerve connections. However, it's still early days and scientists need to do more research to confirm these findings.

TWO MONTHS OLD

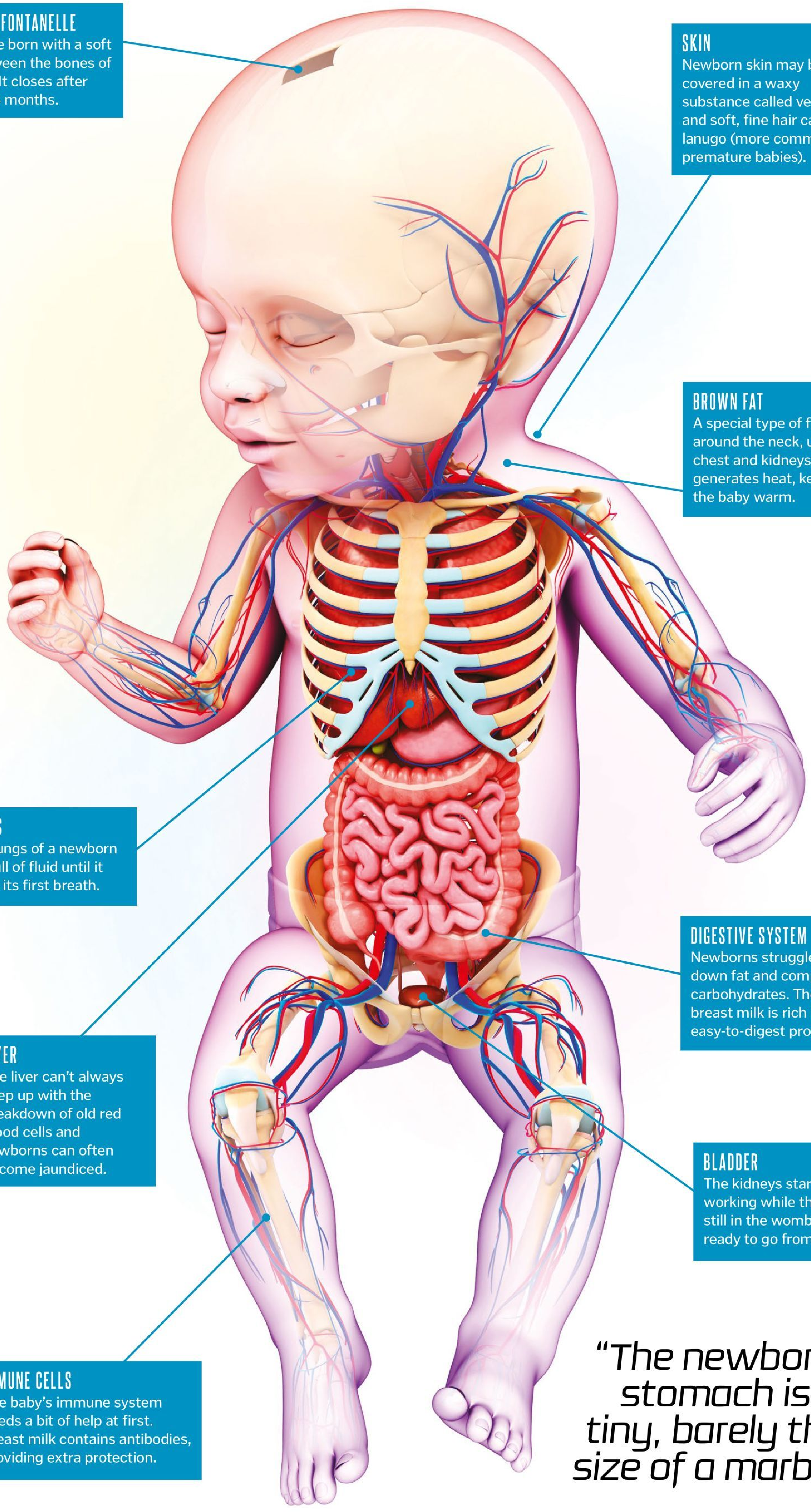
Babies spend much of their time eating and sleeping, and their bodies start to grow rapidly. In the womb, cells divide constantly to form tissues and organs, but after birth growth shifts. Rather than making new cells, babies increase the size of the cells they already have.

The tissues of newborn babies are very different to those of children and adults. There is more fluid around their muscle and nerve cells, and they have less cytoplasm inside. As the baby develops this balance shifts. Muscle cells expand, filling with cytoplasm and molecules involved in contraction. Nerve cells extend, strengthening connections and making new ones, and the amount of fluid outside these cells starts to fall. With newfound strength, babies learn to push up with their hands when placed on their tummies and start to hold their head a little steadier, their movements becoming less jerky and more coordinated.

Fat continues to quickly build up under the skin, helping to keep the infant warm. By the

BABY ANATOMY

BABIES ARE MORE THAN JUST MINIATURE ADULTS – THEY HAVE THEIR OWN UNIQUE ANATOMY



ANTERIOR FONTANELLE
Babies are born with a soft spot between the bones of the skull. It closes after around 18 months.

SKIN
Newborn skin may be covered in a waxy substance called vernix and soft, fine hair called lanugo (more common in premature babies).

BROWN FAT
A special type of fat around the neck, upper chest and kidneys generates heat, keeping the baby warm.

LUNGS
The lungs of a newborn are full of fluid until it takes its first breath.

DIGESTIVE SYSTEM
Newborns struggle to break down fat and complex carbohydrates. The first breast milk is rich in easy-to-digest proteins.

LIVER
The liver can't always keep up with the breakdown of old red blood cells and newborns can often become jaundiced.

BLADDER
The kidneys start working while the baby is still in the womb and are ready to go from birth.

IMMUNE CELLS
The baby's immune system needs a bit of help at first. Breast milk contains antibodies, providing extra protection.

> *"The newborn stomach is tiny, barely the size of a marble"*

© SPL; Thinkstock

two month mark babies are already starting to develop social skills. They begin to follow things with their eyes and recognise people at a distance, and they begin to smile and laugh.

HALFWAY THROUGH

Babies can finally hold their heads steady at around 16 weeks of age. They will also start to push down with their legs if they're held above a hard surface, and by six months they can roll over, push up to a crawling position and even stand with support.

At around this time babies also begin to use their hands and eyes together. They reach for objects and rake with their fingers to grab them, and they start to use their mouths to explore objects further. With all this extra strength and coordination, the grasp and Moro reflexes are no longer needed. These early fail-safes fade away. Babies start to learn to pass toys from one hand to the other.

Their eyesight improves too. By this stage they are becoming more perceptive to the subtleties of different colours, and they start to copy facial movements. They recognise and express emotion and begin to find their voice. They blow raspberries and start to make consonant sounds like 'ba', 'da' and 'ga', using noise to get attention and to express themselves. They will also start to recognise words, especially their own name.

> "To fuel all this progress, six-month-old infants often switch to solid food"

To fuel all this progress, six-month-old infants often switch to solid food. As the baby grows, the fat content of breast milk has been increasing from about 2g/dL of colostrum (grams per decilitre, equivalent to 100 millilitres) to 4.9g/dL. It has provided energy and contributed to a growing store of fat under the skin. But now the digestive system is ready for more.

A newborn's digestive organs are not only smaller than an adult's, but they also work differently. They make different quantities of enzymes and bile and they operate at a different pH. But at six months old things are starting to change. The first teeth come through, starting with the bottom front teeth then the top. Swallowing improves and the digestive system will start to produce enzymes to break down complicated meals.

FIRST BIRTHDAY

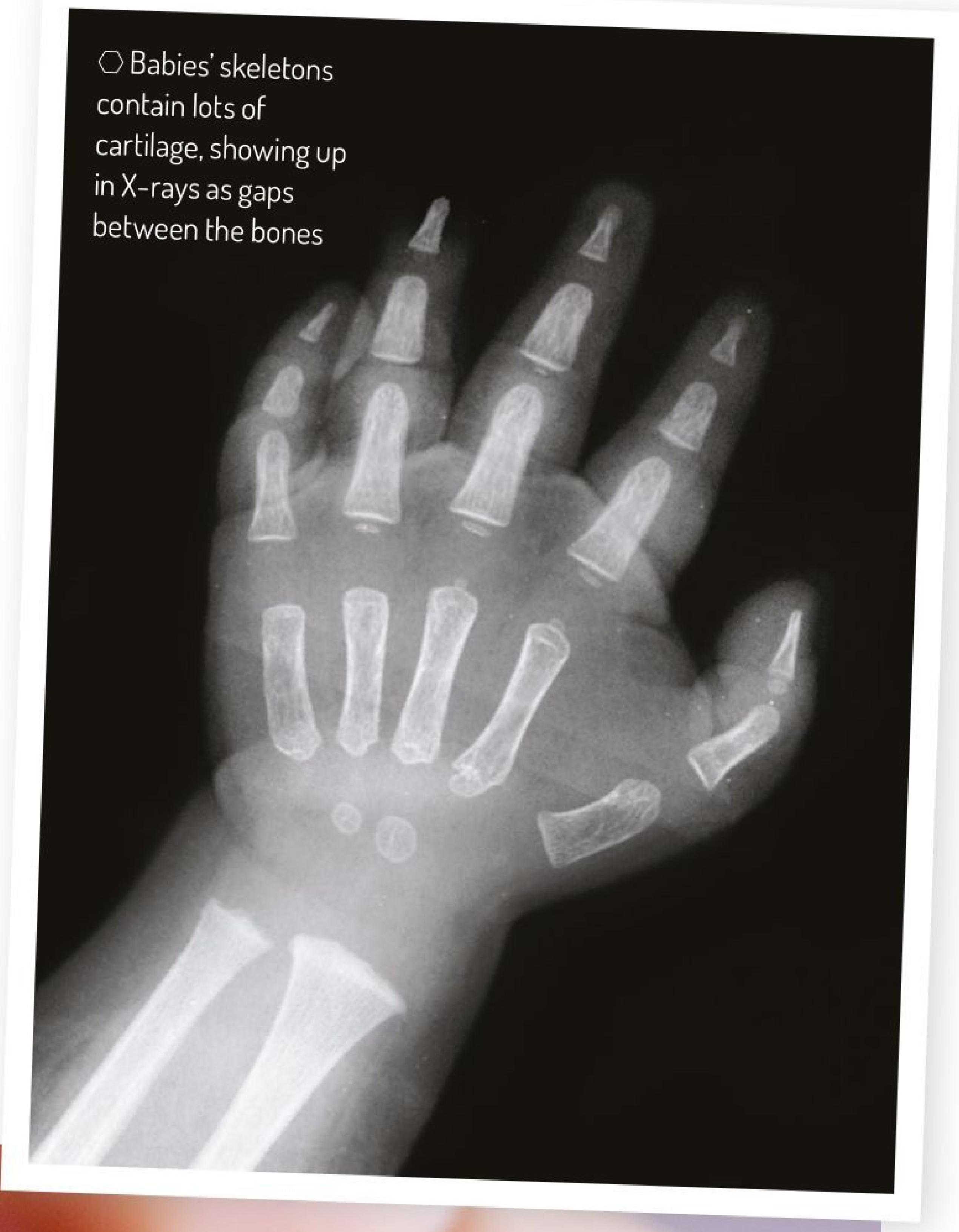
By their first birthday, babies are starting to develop complex behaviours. They have favourite things and favourite people. They start to understand 'object permanence' – the idea that objects and people exist even though you can't always see them. They look for hidden objects and they begin to grasp the effects of gravity by learning to drop things and watching how they fall to the ground.

They also begin to respond to requests and make demands of their own. They will copy and use gestures like waving, pointing and head shaking. By now they will also understand familiar words and follow simple directions, as well as being able to help with tasks like dressing. Most importantly of all, they will start to communicate using 'babble'.

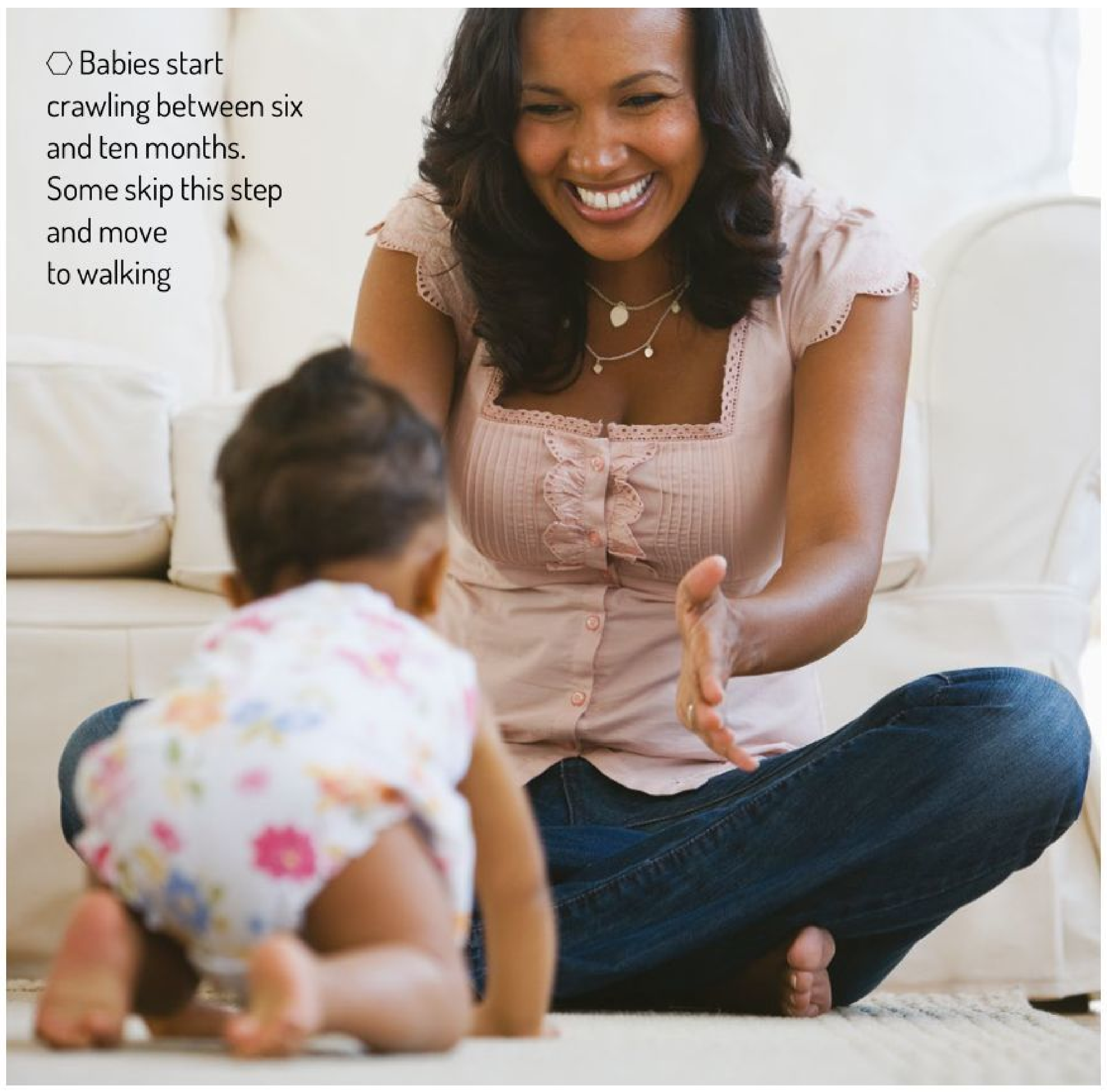
Their coordination has by now improved too. The grasp reflex is long gone, and they can move objects easily from one hand to the other. They can pick up small things between their thumb and forefinger and they will test new objects by shaking and banging. They will begin cruising, holding on to objects and moving around on two legs. Some may even take their first steps.

The hole that shunted blood through the heart when they were born is now fully healed over. Back teeth are starting to come through and the digestive system is processing full meals. The lungs have more air sacs, increasing surface area for gas exchange, and the brain has developed billions upon billions of new connections.

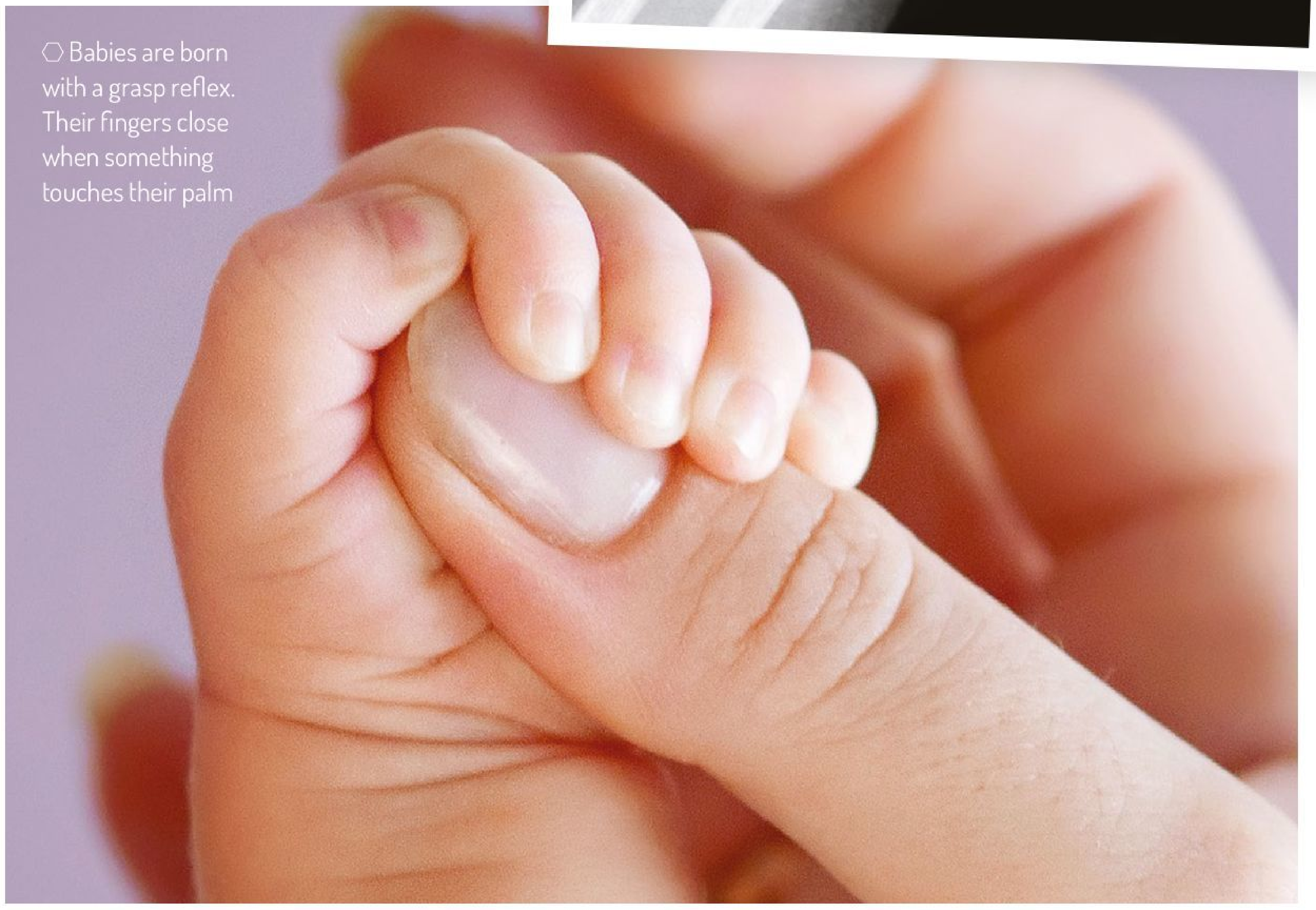
Over the coming months, babies transform into toddlers. As they begin to develop their understanding of the world they start wanting to be more independent. They learn to walk, they start to talk and they even play games. Human babies are born tiny and vulnerable, but in a few short months they are already well on the way to growing up.



Babies' skeletons contain lots of cartilage, showing up in X-rays as gaps between the bones



Babies start crawling between six and ten months. Some skip this step and move to walking

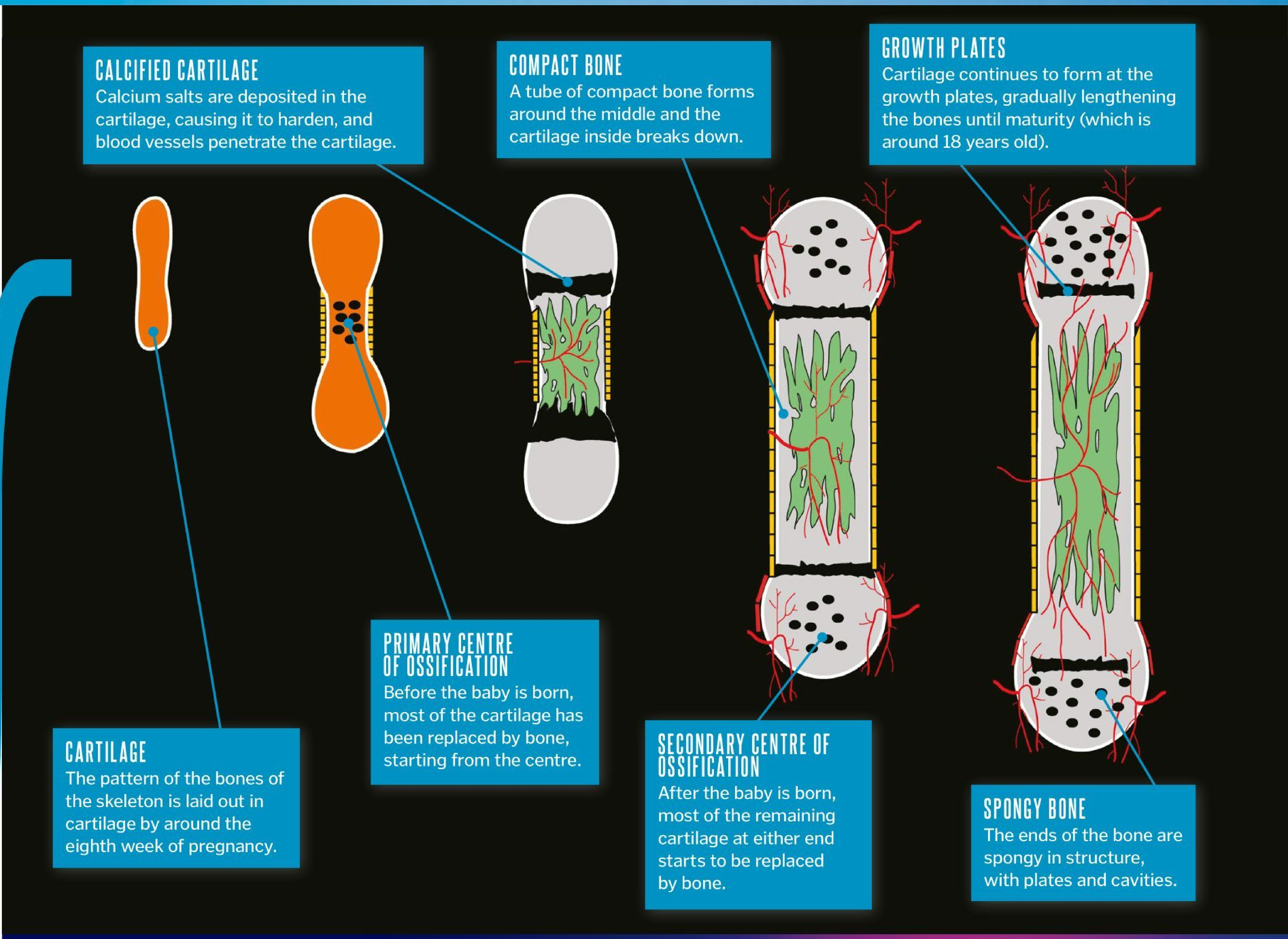


Babies are born with a grasp reflex. Their fingers close when something touches their palm

BRAIN DEVELOPMENT / HOW BONES GROW

SKELETONS START OUT AS CARTILAGE AND GRADUALLY TURN TO BONE

NEWBORN BRAINS GROW FROM 25 TO 90 PER CENT OF ADULT VOLUME IN JUST FIVE YEARS



CALCIFIED CARTILAGE
Calcium salts are deposited in the cartilage, causing it to harden, and blood vessels penetrate the cartilage.

COMPACT BONE
A tube of compact bone forms around the middle and the cartilage inside breaks down.

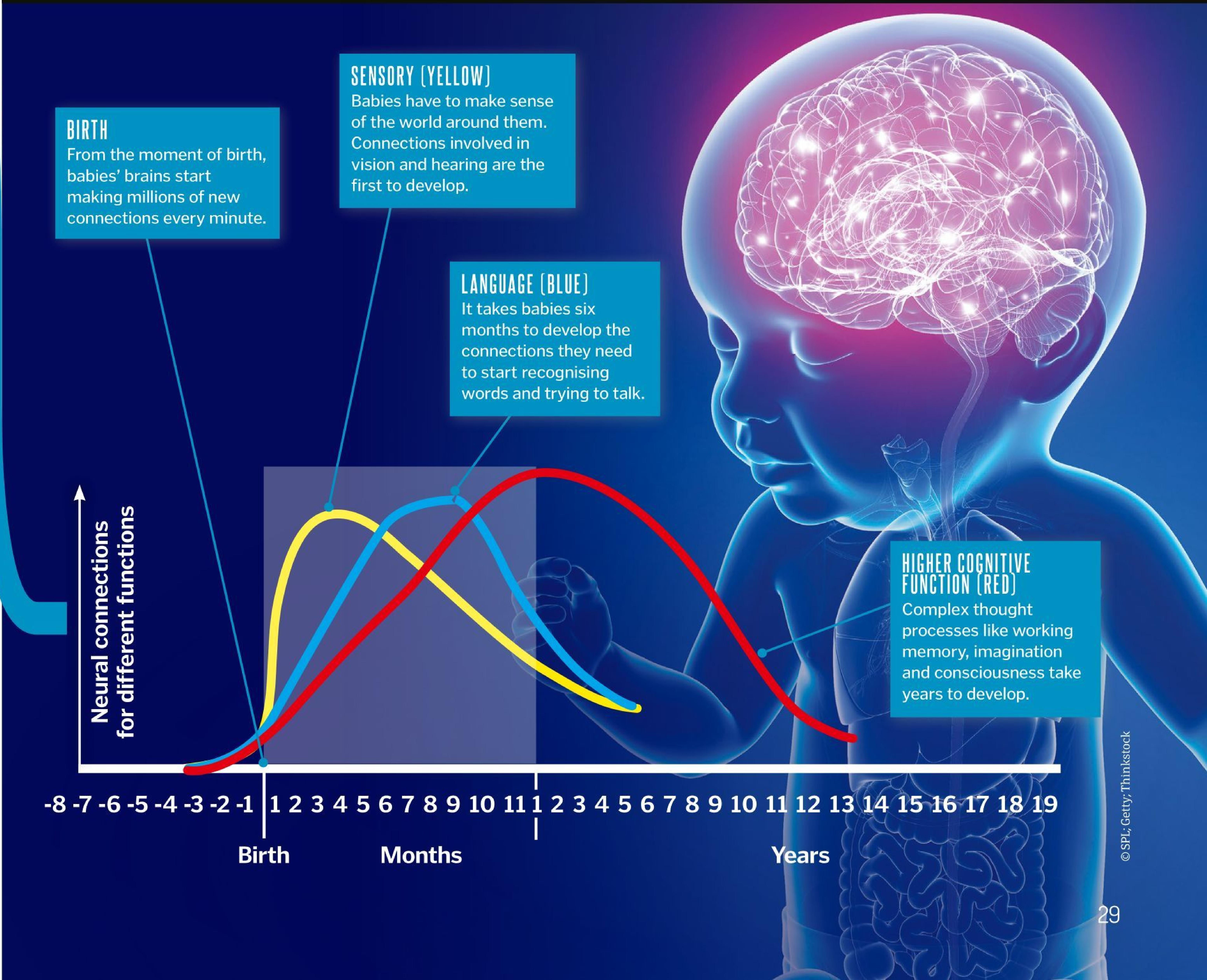
GROWTH PLATES
Cartilage continues to form at the growth plates, gradually lengthening the bones until maturity (which is around 18 years old).

PRIMARY CENTRE OF OSSIFICATION
Before the baby is born, most of the cartilage has been replaced by bone, starting from the centre.

CARTILAGE
The pattern of the bones of the skeleton is laid out in cartilage by around the eighth week of pregnancy.

SECONDARY CENTRE OF OSSIFICATION
After the baby is born, most of the remaining cartilage at either end starts to be replaced by bone.

SPONGY BONE
The ends of the bone are spongy in structure, with plates and cavities.



BIRTH
From the moment of birth, babies' brains start making millions of new connections every minute.

SENSORY (YELLOW)
Babies have to make sense of the world around them. Connections involved in vision and hearing are the first to develop.

LANGUAGE (BLUE)
It takes babies six months to develop the connections they need to start recognising words and trying to talk.

HIGHER COGNITIVE FUNCTION (RED)
Complex thought processes like working memory, imagination and consciousness take years to develop.

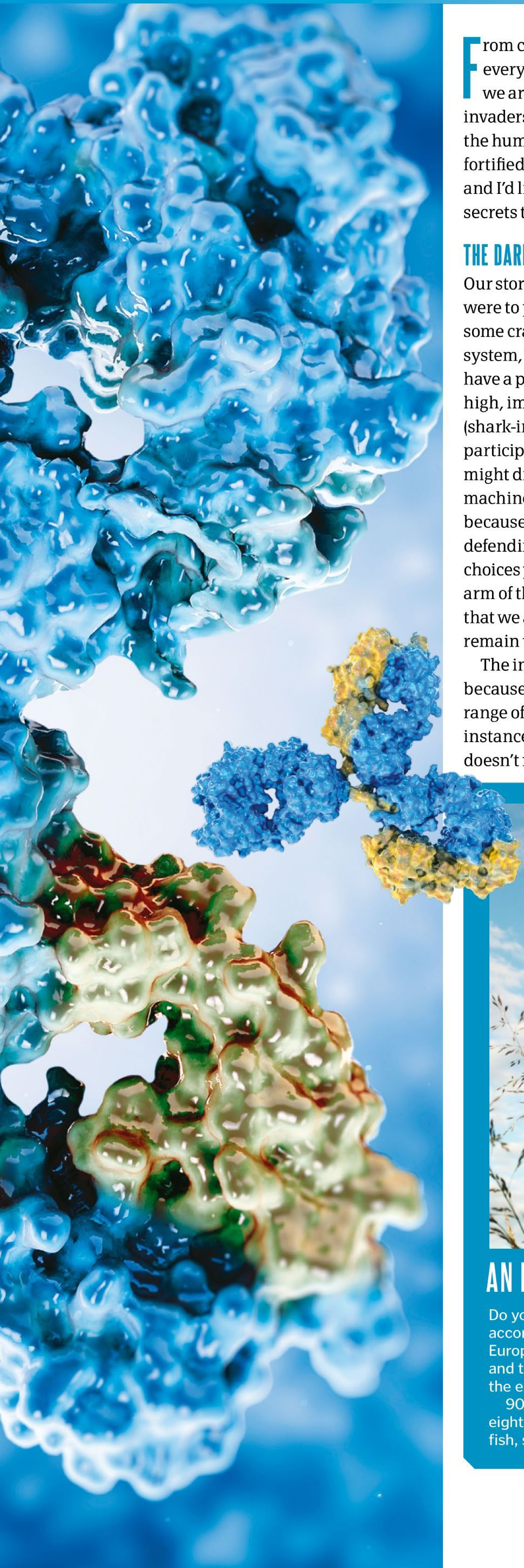
© SPL; Getty; Thinkstock

THE IMMUNE SYSTEM

YOUR BODY UNDER SIEGE – DISCOVER HOW YOUR IMMUNE ARMY DEFENDS AND PROTECTS YOU

MEET THE EXPERT

Dr Catherine Carver is a writer and recovering medic and academic. She completed a Master's degree at Harvard and was shortlisted for the *Guardian*'s 2012 Science Writing Prize. Her first book, *Immune*, offers a fun-filled journey through the immune system.



From cleaning the kitchen sink to having sex, everything we do exposes us to invaders. Yet we are safe. Most of the time potential invaders' attempts are thwarted. This is because the human body is like an exceedingly well-fortified castle, defended by billions of soldiers, and I'd like to reveal its myriad of miracles and secrets to you.

THE DARK ARTS OF THE INNATE DEFENCES

Our story begins with a feat of imagination: if we were to put 100 people in a room, hand them some crayons and ask them to draw a defence system, what might you expect to see? You can have a pretty good guess – probably castles with high, impenetrable walls surrounded by moats (shark-infested, among the more creative participants). A less historically inclined artist might draw us an array of lasers, rockets and machine guns. These are relatively predictable because even without knowing what you're defending against, there are certain solid choices you can make. This is akin to the 'innate' arm of the immune system – the set of defences that we are born with and which essentially remain the same throughout our lives.

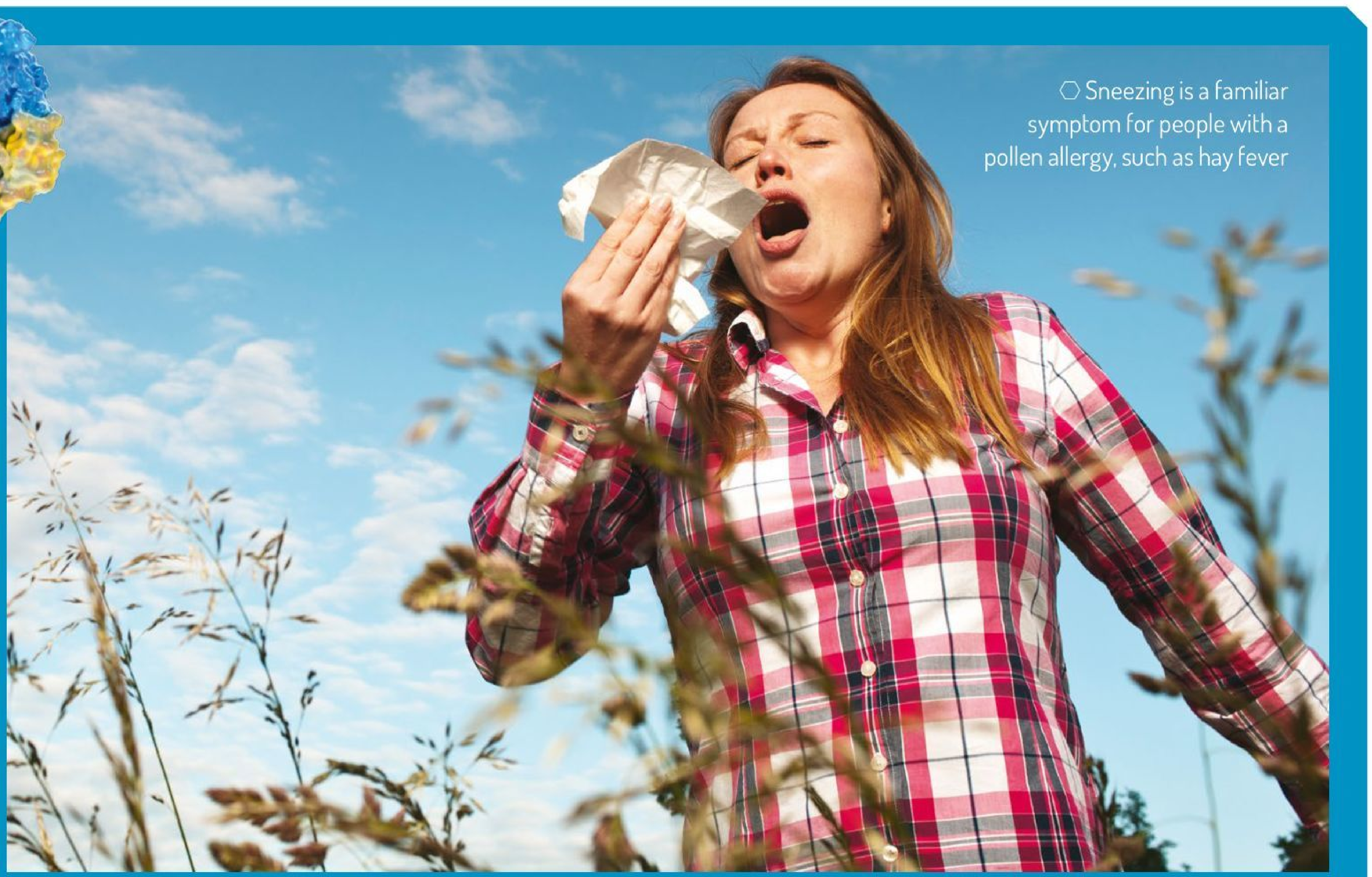
The innate system is the first line of defence because it's already set up and ready to take on a range of common pathological patterns. For instance, all invaders need an entry point – it doesn't matter if you're a tiny virus or a massive worm, you need a way in – so part of the innate immune system's role is to maintain robust control of the body's entry and exit points.

Cue our first innate defence: skin. Skin is the largest human organ; if you were to peel yours off you'd lose about 12 kilograms instantly. The skin on the soles of your feet is eight-times thicker than the skin on your eyelids, but every inch of it is an exquisite barrier that keeps unwanted invaders out.

While snakes shed their skins in one go, we slough off old skin continuously and rain it down at a rate of roughly 50,000 cells a minute. Given that fact, it's almost unsurprising that dead skin accounts for about a billion tons of dust in the atmosphere. Unsurprising, but gross. On the plus side, this constant turnover of cells means the barrier is continually replenished, keeping our skin healthy and keeping the billions of bacteria slathered over its surface out.

Unfortunately, we can't be truly impenetrable. We need to let in food and water and air and light, and we need to let some things out, too. So we have a body full of holes, which is deeply inconvenient from a security perspective. But we have clever holes. Take your mouth: every time

> "The innate system is the first line of defence"



○ Sneezing is a familiar symptom for people with a pollen allergy, such as hay fever

AN EPIDEMIC OF ALLERGIES

Do you have any allergies? If so, you're not alone; according to Allergy UK, "More than 150 million Europeans suffer from chronic allergic diseases, and the current prediction is that by 2025 half of the entire EU population will be affected."

90 per cent of food allergies are caused by just eight things: milk, eggs, peanuts, nuts from trees, fish, shellfish, soy and wheat. All of these allergies are caused by the immune system reacting to a harmless substance by launching an unwarranted attack that can cause symptoms from a rash to a life-threatening airway blockage.

While we don't know why the immune system does this, we do know some people are more genetically susceptible to allergies because they run in families.

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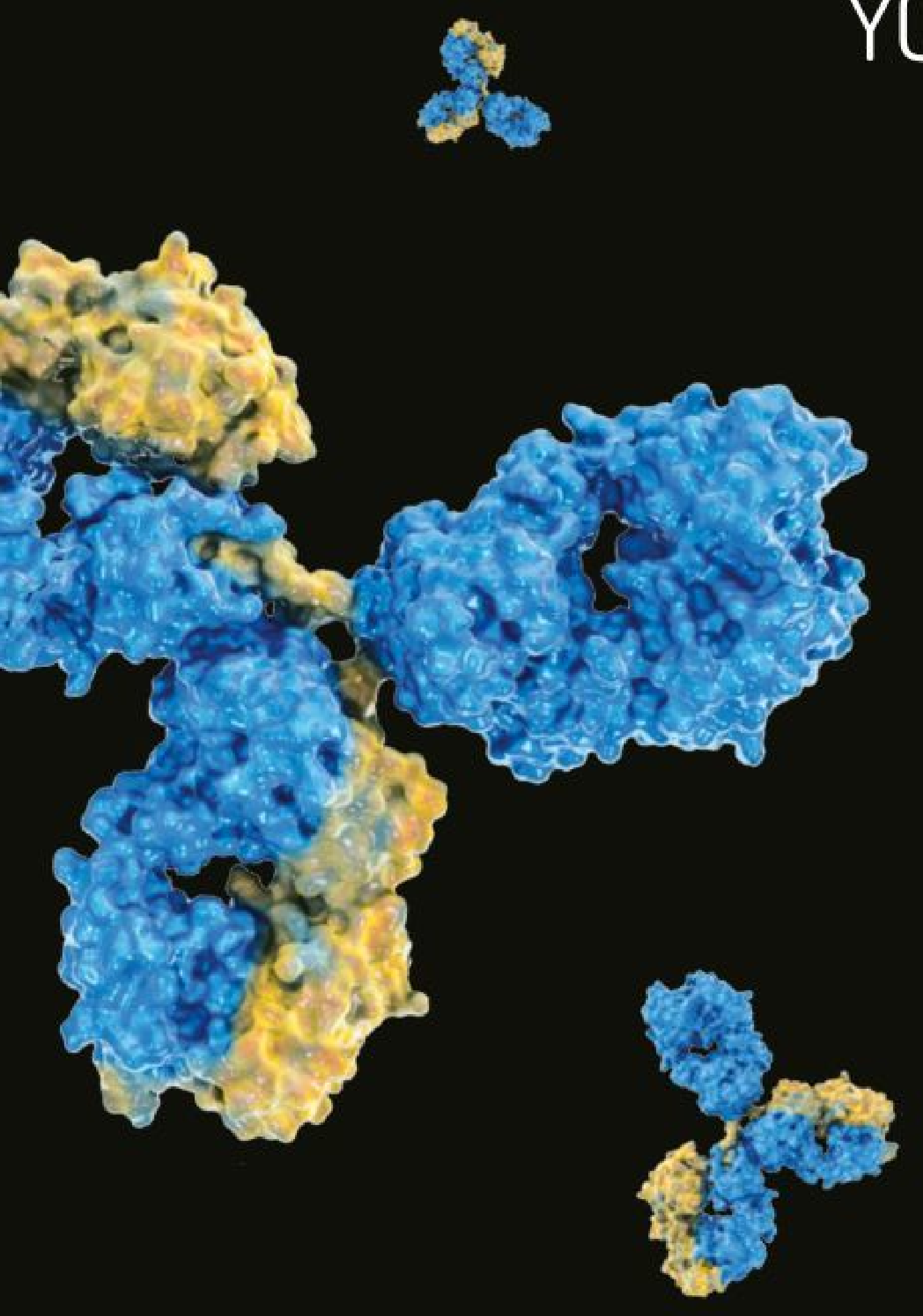
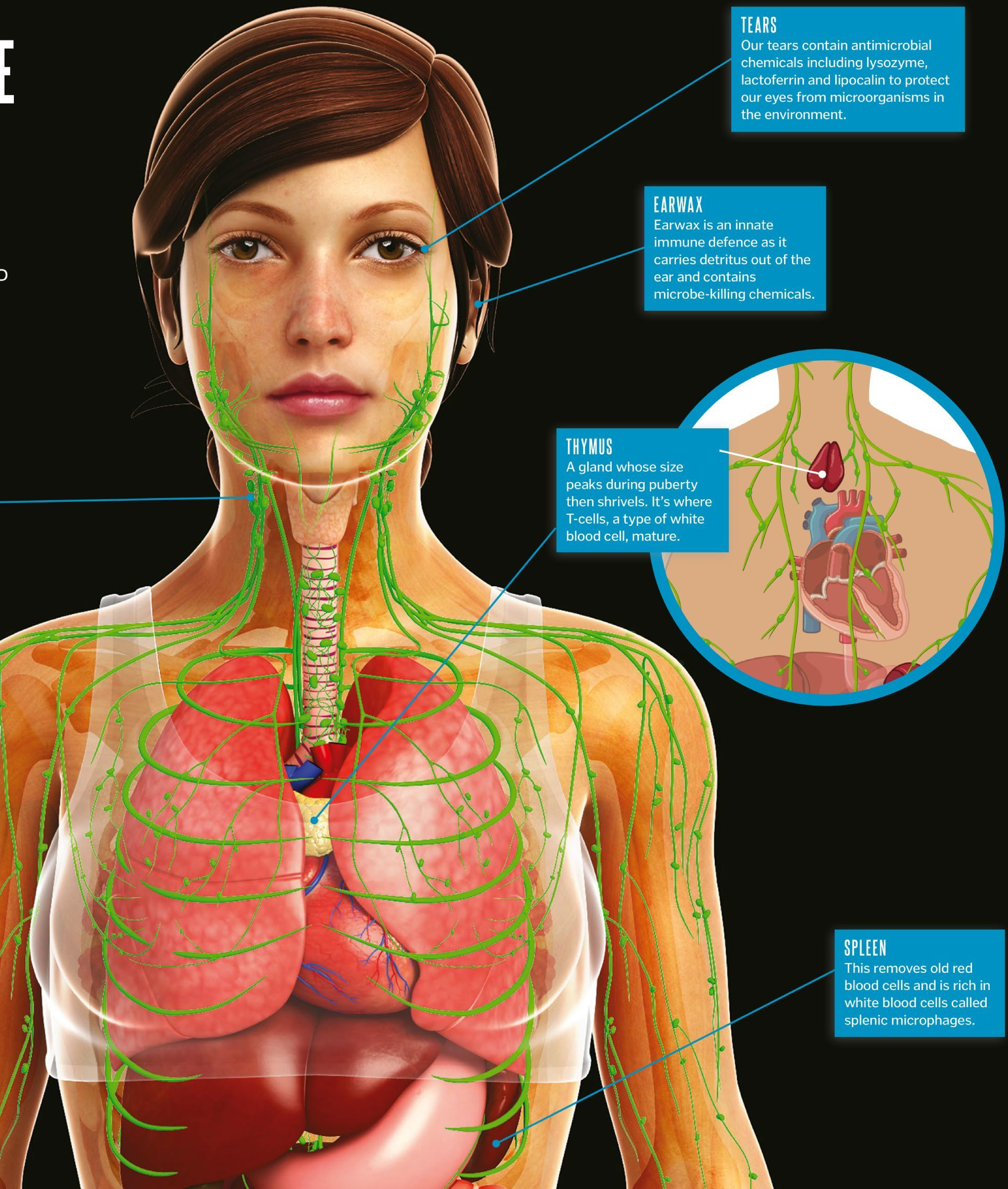
YOUR IMMUNE SYSTEM

DISCOVER SOME OF THE DIFFERENT ORGANS AND COMPONENTS THAT MAKE UP YOUR BODY'S DEFENCES





TEARS
Our tears contain antimicrobial chemicals including lysozyme, lactoferrin and lipocalin to protect our eyes from microorganisms in the environment.

EARWAX
Earwax is an innate immune defence as it carries detritus out of the ear and contains microbe-killing chemicals.

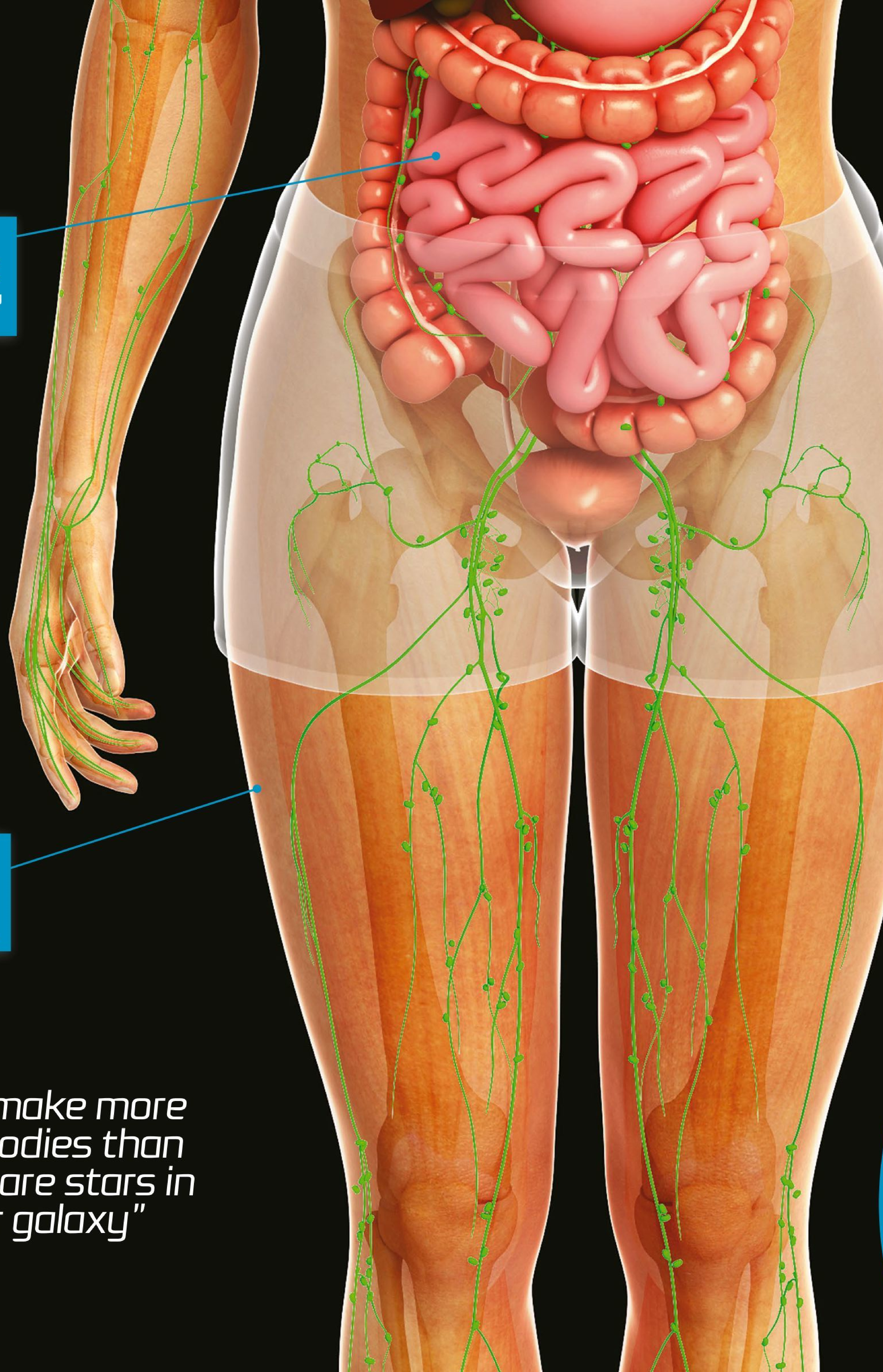
LYMPH NODES
This is where special white blood cells can be presented with foreign material like bacteria and set off to kill it.

THYMUS
A gland whose size peaks during puberty then shrivels. It's where T-cells, a type of white blood cell, mature.

SPLEEN
This removes old red blood cells and is rich in white blood cells called splenic microphages.

URGENT
HUMAN
ORGANS

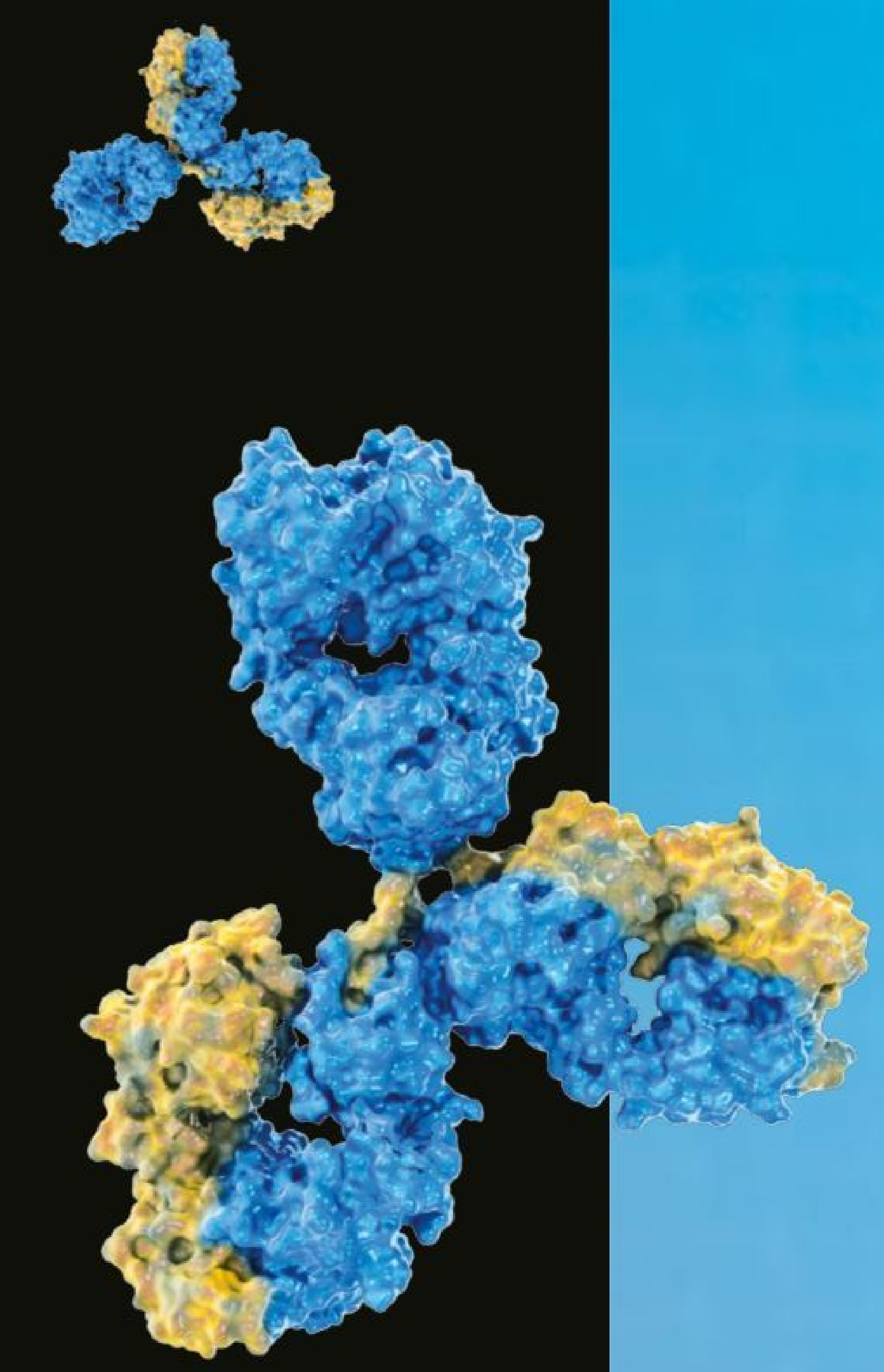
○ The immune system is critical to the success or failure of organ transplants



INTESTINE
Contains Peyer's patches, tissue that can act like an alert system for detecting intruders in the gut.

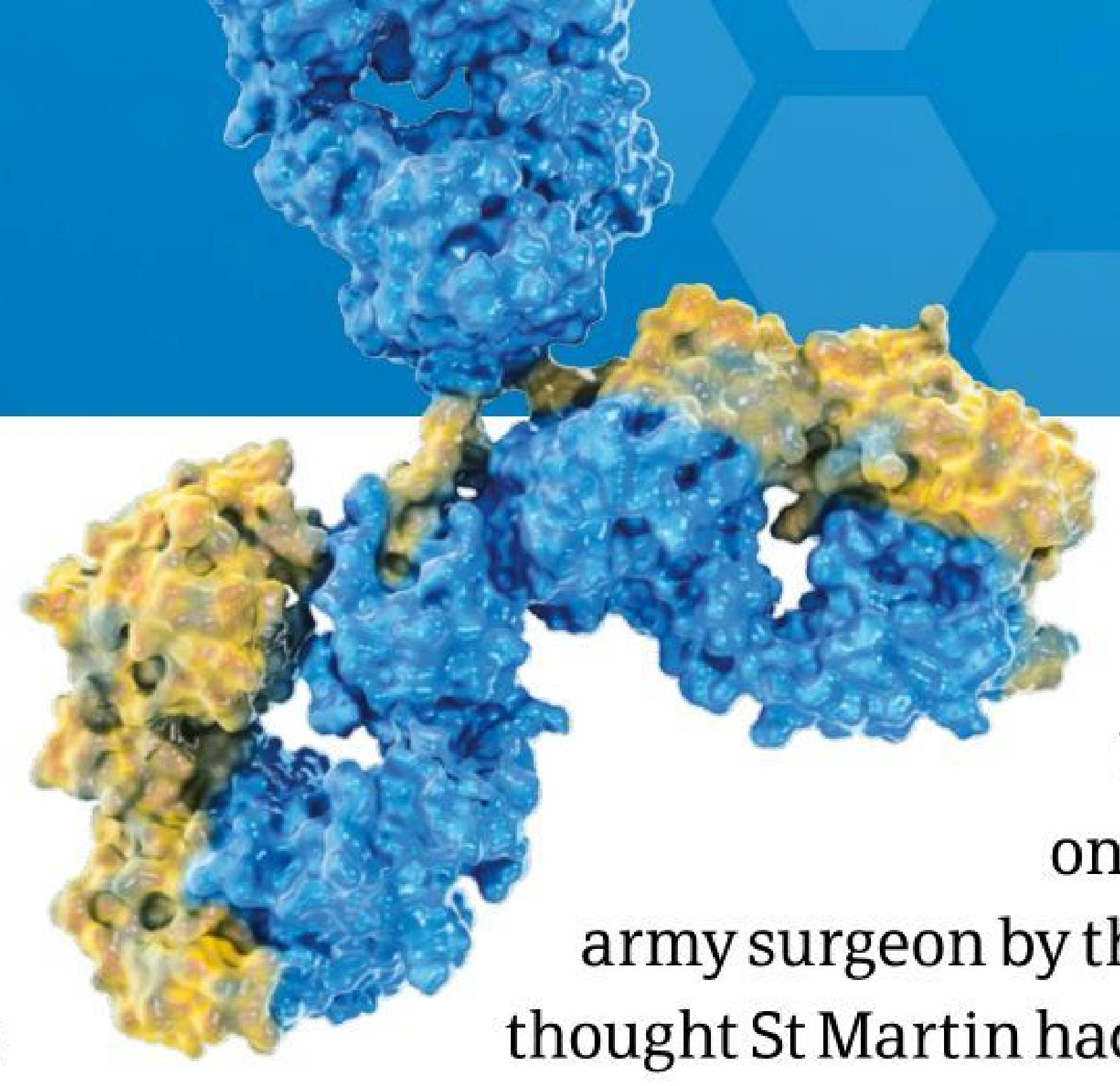
SKIN
Skin is an essential part of the immune system, keeping potentially dangerous microbes out.

LYMPHATIC VESSELS
An unidirectional transport network that's a key way for white blood cells to travel the body.



> *"We make more antibodies than there are stars in our galaxy"*

⬡ Skin is an essential defence, keeping out a multitude of microbes



you inhale you are sucking about 10,000 bacteria into your lungs. Thankfully, your airways are exceedingly well booby-trapped passages lined with goblet cells, which secrete a fine layer of mucus to trap dirt and bacteria. The dirty mucus is then escorted out by microscopic whip-like structures called cilia, which stick out from the lining of the airways and beat 1,000–1,500 times per minute, forcing the mucus up and out of the lungs in waves at a rate of two to three centimetres per minute.

While the lung escorts invaders out in an orderly fashion, the gut takes a more medieval approach to border control: acid. This acid is the reason the normal stomach is an unwelcoming pH 2, capable of disintegrating many of the microorganisms that land in it. The discovery of this acid has a rather gruesome history.

The story begins in June 1822 on the island of Michilimackinac in the wilds of Michigan. At the time this lush green island, christened 'the great turtle' by the Ottawa and Chippewa tribes, was the main trading post of the American Fur Company (the brainchild of America's first multimillionaire, John Jacob Astor).

It was while standing in line at the Fur Company store that a 20-year-old trapper by the name of Alexis St Martin was accidentally shot. The only doctor on the island arrived to a scene worthy of any horror movie – "a portion of the lungs as large as a turkey's egg protruding through the external wound". St Martin also had a hole in his stomach through which his breakfast was spilling out on to his shirt. His doctor, an army surgeon by the name of Beaumont, thought St Martin had little chance of survival but astoundingly, with the care of Beaumont, St Martin slowly became whole again. Well, almost. The hole in his stomach didn't fully heal, and St Martin declined offers from Beaumont to stitch it shut. This physical quirk changed not only the course of their relationship but also the history of science.

Over the course of several years and 238 experiments, Beaumont extracted acid and introduced medicine and food into the hole in St Martin's stomach. This led to Dr Beaumont's seminal publication on the subject, including conformation that hydrochloric acid is the most important acid in the stomach.

David Vetter lived life in a bubble because he didn't have an immune system to defend him

> "The immune system influences everything from pregnancy to organ transplantation"

ADAPTIVE ASSASSINS

Let's imagine a different task from our original artistic efforts. If we had given our 100 people the challenge of drawing a defence system against a very specific threat, they would have drawn rather different defences. For instance, garlic and holy water would be essential in an anti-Dracula defence system but would be frankly embarrassing in the face of Darth Vader. This opponent-specific weapons selection resembles the 'adaptive' arm of our immune response, which complements the breadth of the innate response by being able to recognise and respond to specific threats.

Included within the adaptive system are antibodies, which are Y-shaped proteins that can latch onto bacteria, parasites and viruses and label them for destruction by our white blood cells.

Our ability to make a diverse array of antibodies is legendary. We can make over 1 trillion different antibodies – that's more antibodies than there are stars in our galaxy. Making this level of diversity means that, given enough time, our body can develop antibodies

AUTOIMMUNE DISEASES

Sometimes, the immune system turns on the very body it's designed to protect. We don't know why, but white blood cells can fail to recognise the body's own cells as belonging to it. The classic example is type 1 diabetes, where the immune system attacks the pancreas.

By systematically destroying the beta cells of the pancreas, the immune system renders the body incapable of making insulin, a hormone essential to controlling blood sugar levels. A diabetic person must use frequent blood tests and synthetic insulin to reduce the risk of serious consequences, including going blind or needing to have limbs amputated.

The severity and commonality of this disease is inspiring many innovative solutions, including in the US, where a bionic pancreas is currently under development.

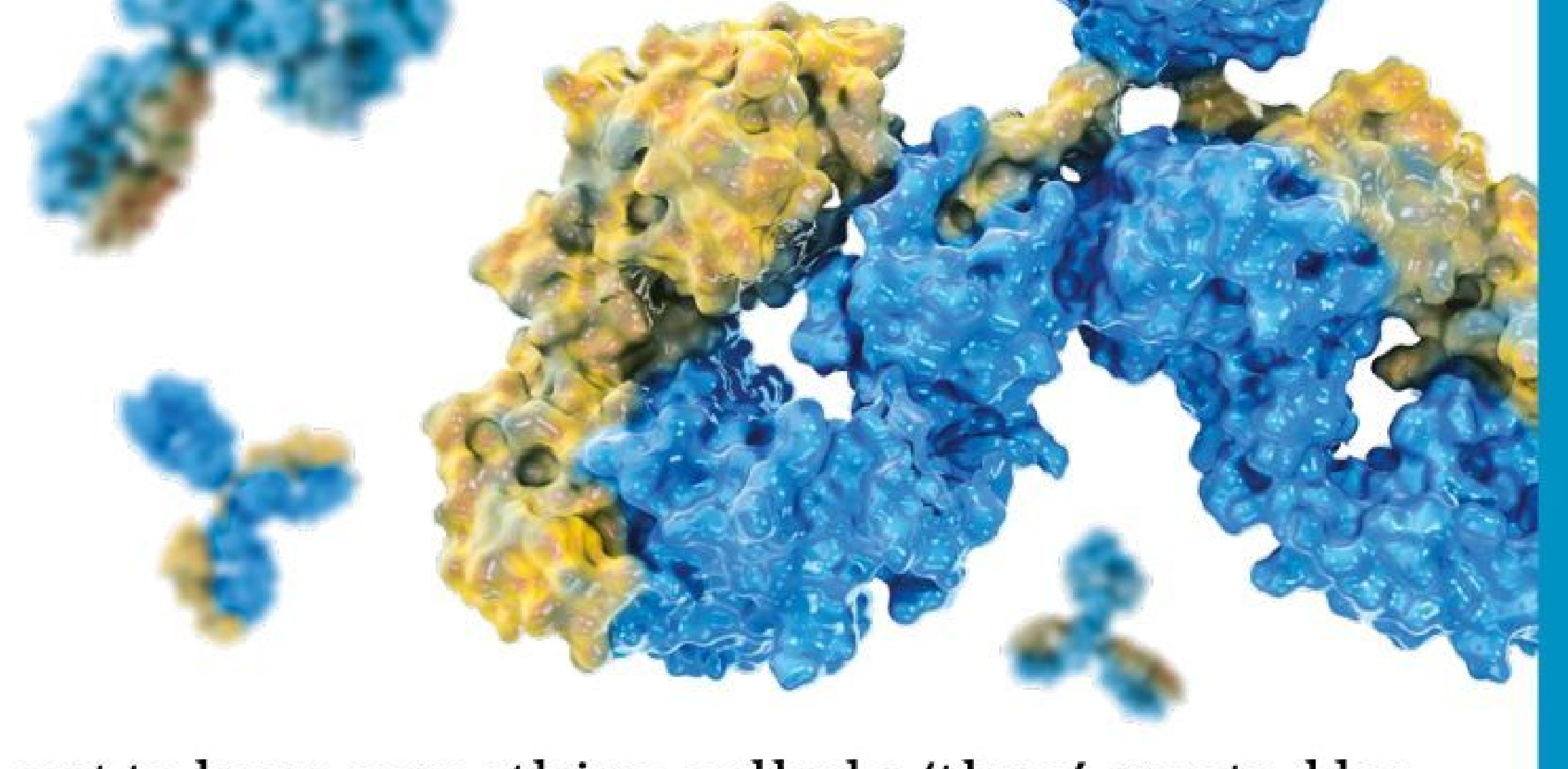
2:35PM
93
mg/dl
M

A diabetic person must use frequent blood tests and synthetic insulin to control their disease

○ Stomach acid has a pH of 2 and is a key innate defence

against everything from the common cold to the Black Death.

Alas, sometimes infections move too quickly and kill us before we have a chance to develop tailored antibodies. Other infections change their shape to evade our adaptive immune response. HIV is well known for it's ability to mutate, changing its surface shape and making it exceedingly difficult for our immune system to make new antibodies quick enough to adapt to HIV's changing face.



TRANSPLANTS

The immune system not only defends and protects us; it also plays a key part in a range of life experiences, from pregnancy to organ transplantation. For example, research suggests the immune system may play a key part in whether a fertilised egg safely implants into the womb and therefore whether a pregnancy proceeds or tragically ends in miscarriage.

In the example of transplants, our immune system can recognise the new organ as foreign and damage it until it can't function, a process called rejection. One option to attempt to avoid transplant rejection is to use cells from the recipient's own body, known as 'self-cells', because the immune system won't see the new tissue as foreign and attack it. For instance, people who lose a thumb can understandably struggle with using their hand. Some therefore opt to have something called a 'thoe' created by transplanting their big toe onto their hand. This may sound unusual but the thoe improves the range of movements the hand can achieve without being a massive loss to the foot.

An even more impressive application of using self-cells to help avoid rejection comes from a rather more intimate area. In 2014, doctors from Mexico and the US operated on four young women affected by Mayer-Rokitansky-Küster-Hauser Syndrome (MRKHS). This rare syndrome causes girls to be born with a completely or partially absent vagina. The surgeons in this case took cell samples from each patient and then grew these cells on a bespoke biodegradable scaffold. After an average of 6.75 years of follow up, all four young women were happy with their transplants, and none were rejected by their immune systems.

DEFENCELESS

When we consider things like transplant rejection, the immune system can seem more like a foe than a friend. However, the tale of David Vetter, a boy without a functioning immune system, is a stark reminder of how dependent we are on our defences.

David was in this world for just 20 seconds before he was transferred to a sterile bubble, where he spent the rest of his life to protect him from the microbes in the environment that would have killed him within days. Sadly he died at the age of just 12 when a failed bone marrow transplant gave him an infection. He never got to drink Coca Cola, one of his life aspirations, and the closest he got to playing in the garden depended on a $50,000 (£38,780) NASA-engineered suit, which he was only able to use six times before outgrowing it.

As David's story tragically reminds us, our defences are absolutely essential to keeping us alive. It is thanks to our immune systems that we are not just alive but thrive in this dirty, beautiful, bug-filled world.

IMMUNOLOGY, SEX AND DEATH

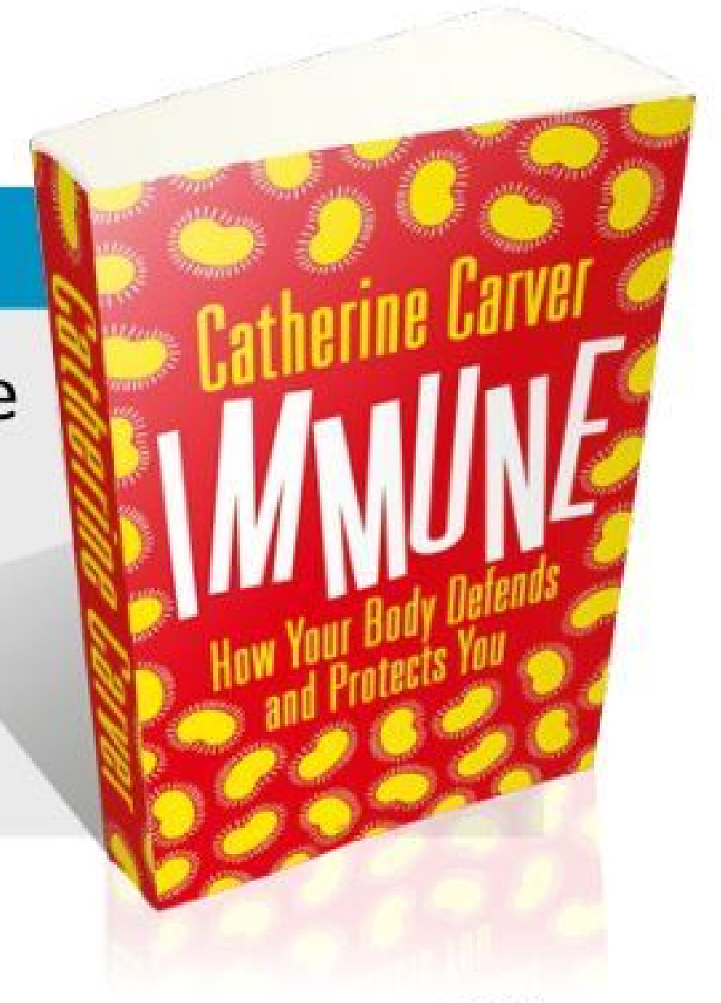
Pity the poor male brown antechinus, a small marsupial found in southeast Australia. In preparation for the short breeding season he stops making sperm and his testes disintegrate, leaving him with stores of sperm and a need to procreate. And so he does, spending up to 14 hours a day mating. But all this comes at a cost in the form of massively raised levels of cortisol, a stress hormone.

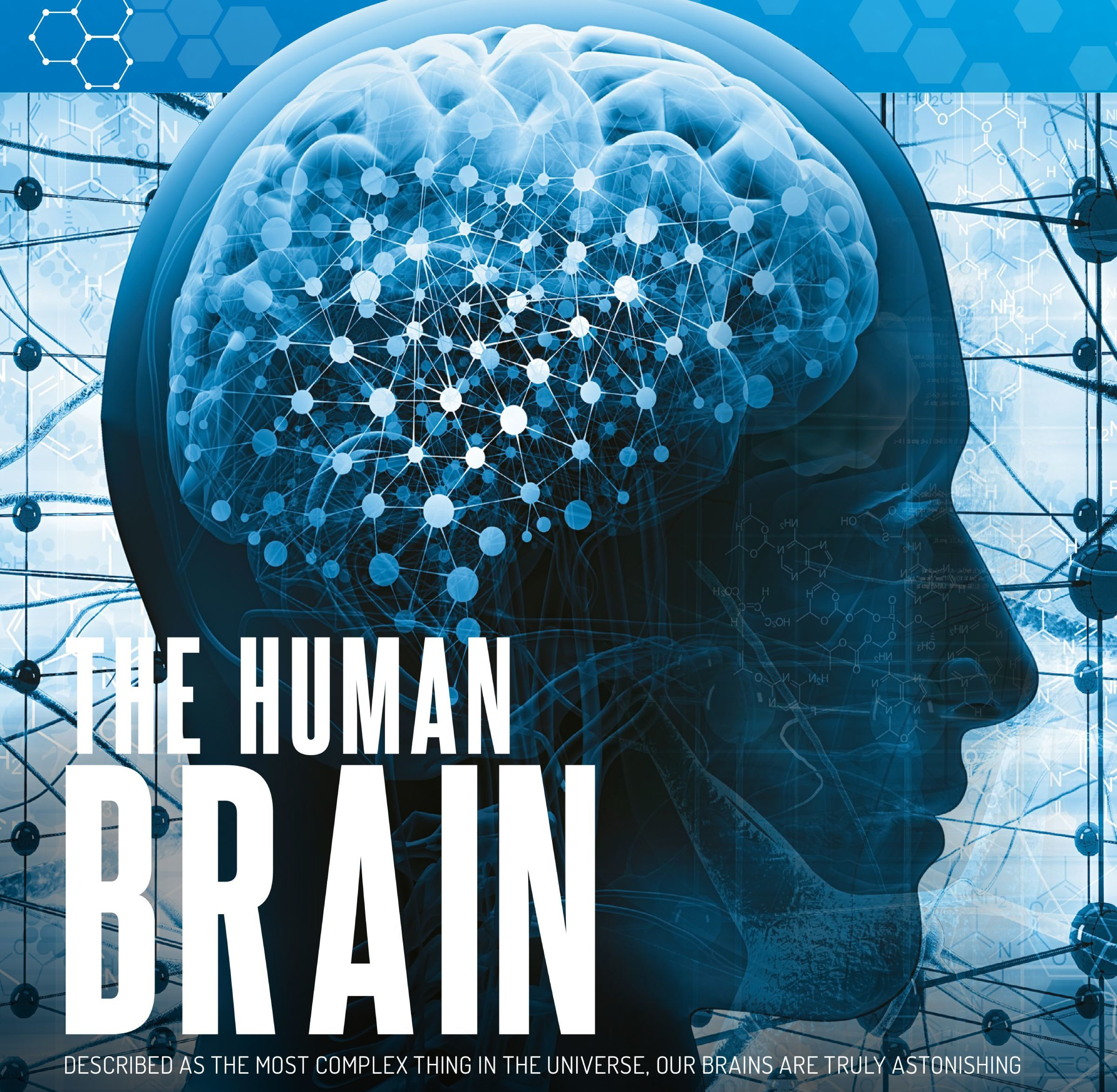
High cortisol leads to severe suppression of immune messenger chemicals, which means that when a male brown antechinus gets injured or ill it can't mount an immune response. This ultimately leads to the death of our valiant, virile little friend.

○ The male brown antechinus goes on a mating frenzy that ultimately ends in his demise

LEARN MORE

For more fascinating facts about the immune system, Catherine's book *Immune: How Your Body Defends and Protects You*, is out now, published by Bloomsbury Sigma.





THE HUMAN BRAIN

DESCRIBED AS THE MOST COMPLEX THING IN THE UNIVERSE, OUR BRAINS ARE TRULY ASTONISHING

The brain makes up just two per cent of our total body weight, but crammed inside are approximately 86 billion neurons, surrounded by 180,000 kilometres of insulated fibres connected at 100 trillion synapses. It's a vast biological supercomputer.

The cells in the brain communicate using electrical signals. When a message is sent, thousands of microscopic channels open, allowing positively charged ions to flood across the membrane. Afterwards, more than 1 million miniature pumps in each cell move the ions back again ready for the next impulse.

The cell bodies of the neurons, and their connections, are contained within the grey matter, which consumes 94 per cent of the oxygen delivered to the brain. Different areas are responsible for different functions, and wiring them together is a fatty network of fibres called white matter.

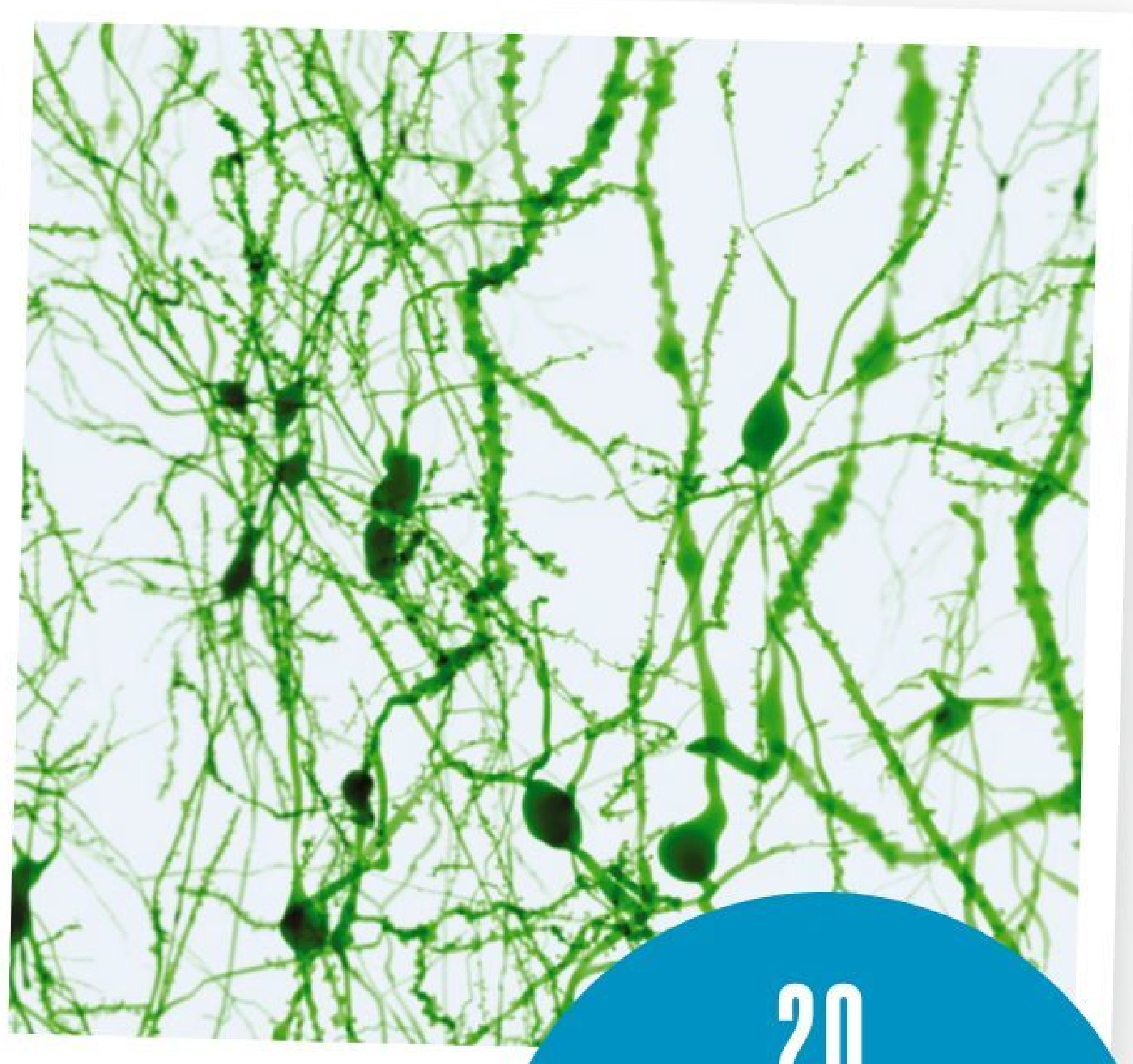
When a signal reaches the end of a nerve cell, tiny packets of chemical signals spill out onto the surrounding neurons. These connections, called synapses, allow messages to be passed from one cell to the next. Each neuron can receive thousands of inputs, coordinating them in time and space, and by type of chemical, to decide what to do next.

Scientists have been electrically and chemically stimulating the brain to see how it responds to different signals, recording electrical activity to map thoughts and using imaging like functional MRI to track the blood flow increases that reveal when nerve cells are firing. The cells of the brain can also be studied inside the lab. Thanks to these investigations we know more about this incredible structure than ever before, but our understanding is only just beginning. There is so much more to learn.

BRAIN DEVELOPMENT

FROM A SINGLE CELL TO AN INCREDIBLY INTRICATE NETWORK IN JUST NINE MONTHS

Within weeks of fertilisation, neural progenitors start to form; these stem cells will go on to become all of the cells of the central nervous system. They organise into a neural tube when the embryo is barely the size of a pen tip, and then patterning begins, laying out the structural organisation of the brain and spinal cord. At its peak growth rate, the developing brain can generate 250,000 new neurons every minute. By the time a baby is born, the process still isn't complete, but by the age of two the brain is 80 per cent of its adult size.



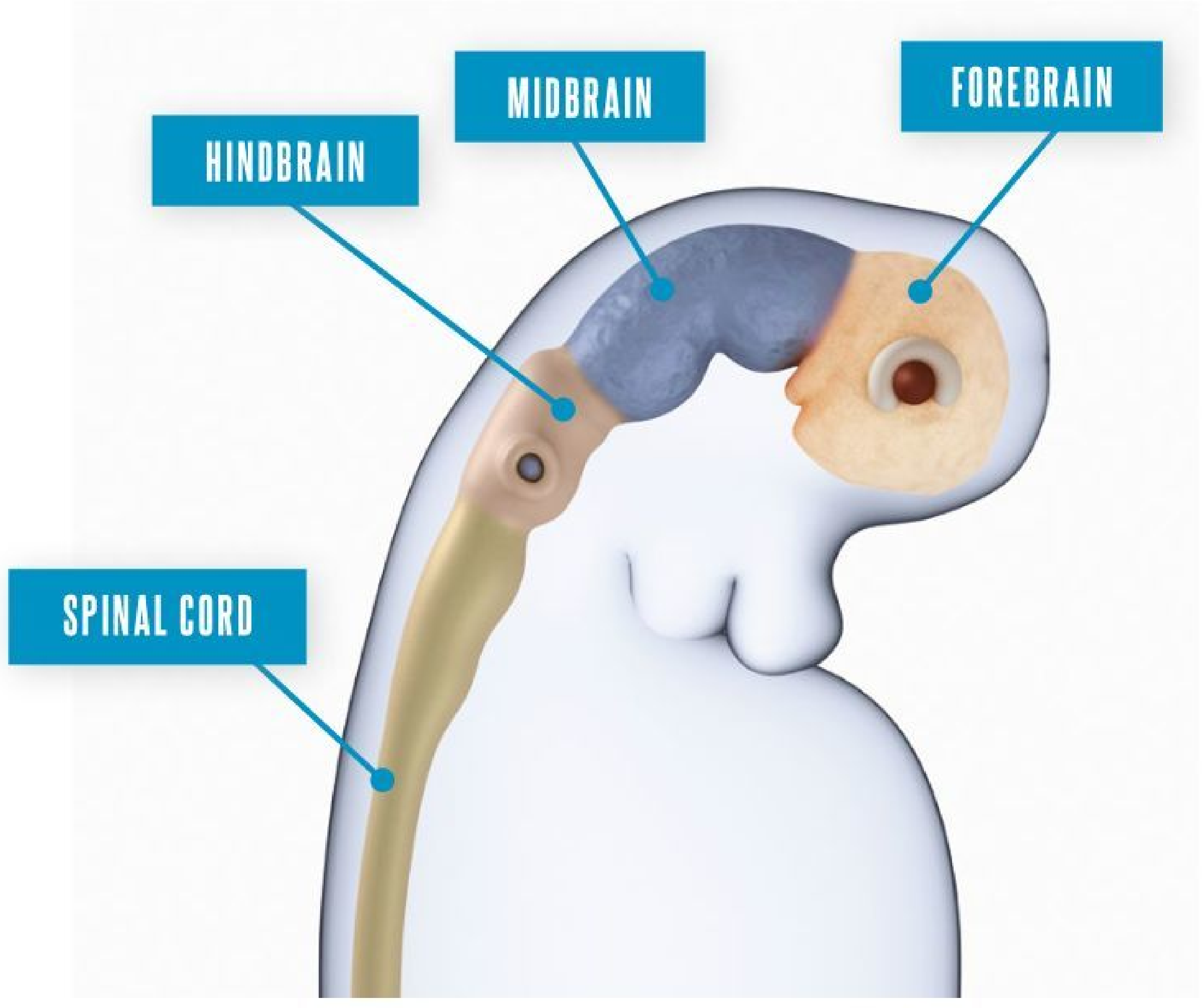
○ Pyramidal neurons, like these, are found in the hippocampus, cortex and amygdala

20 WATTS

Your brain is incredibly efficient, using less energy than a standard lightbulb.

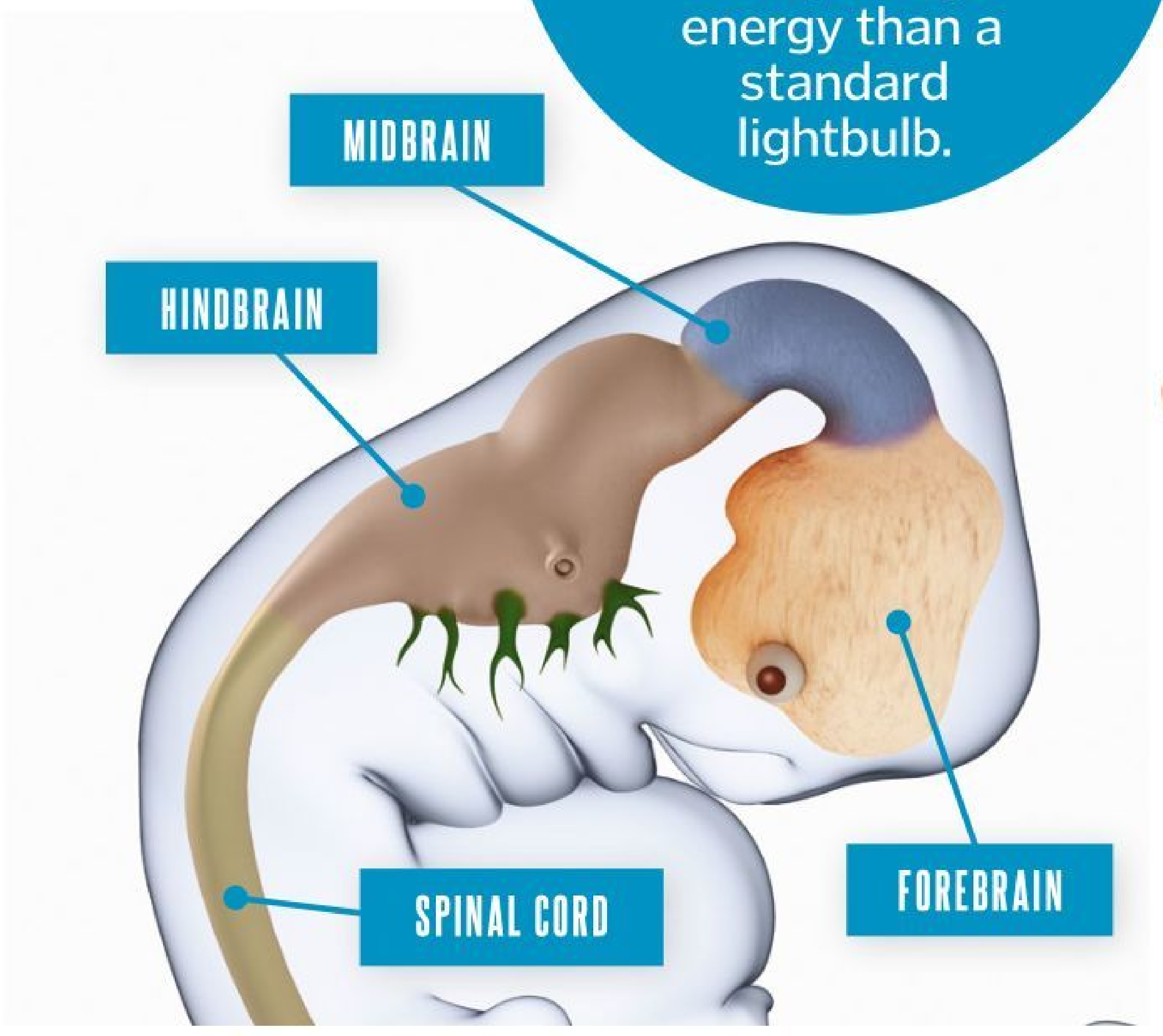
BRAIN FORMATION

THIS ASTONISHING STRUCTURE IS FORMED AND REFINED AS PREGNANCY PROGRESSES



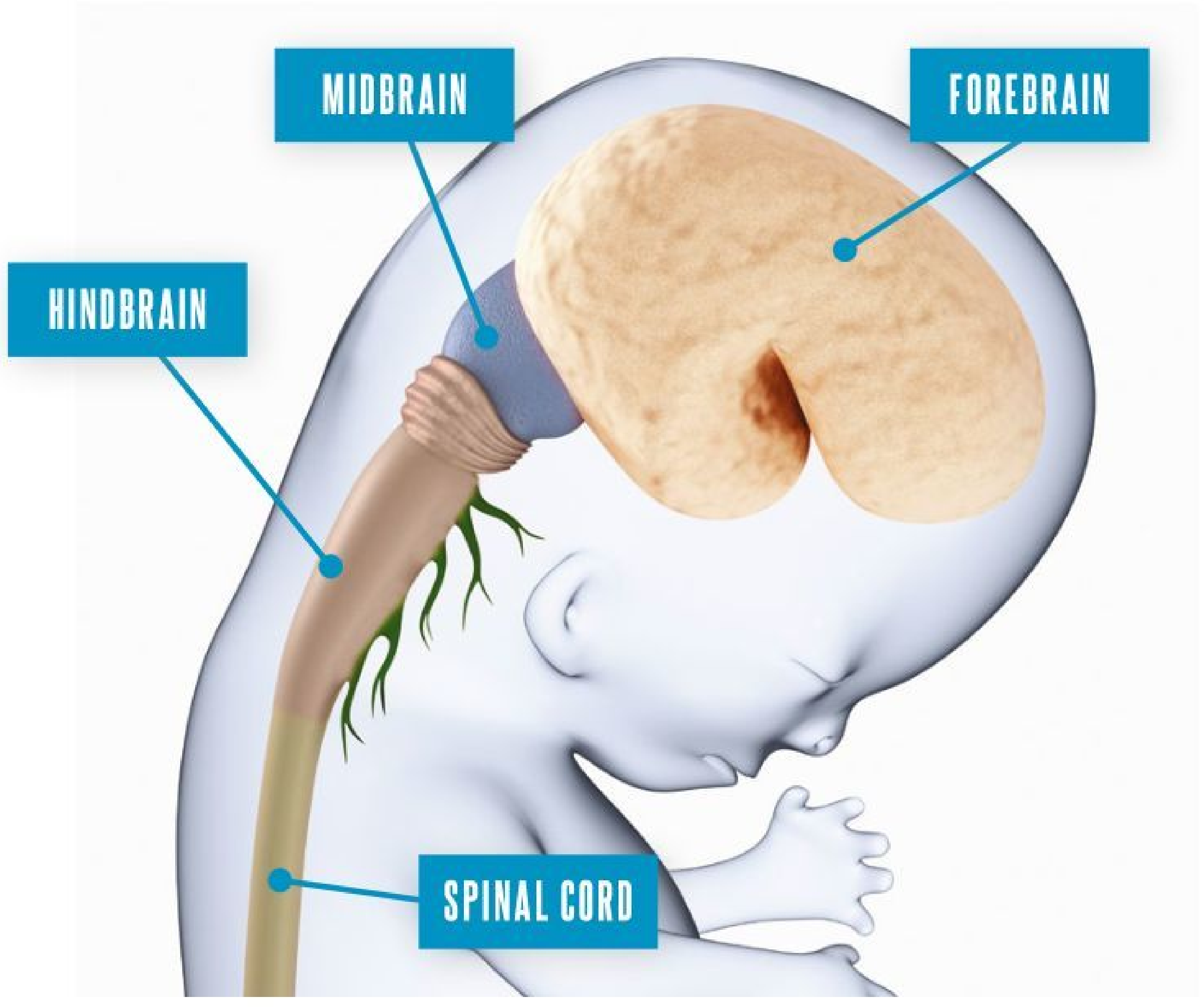
4 WEEKS

Brain development starts just three weeks after fertilisation. The first structure is the neural tube, which divides into regions that later become the forebrain, midbrain, hindbrain and spinal cord.



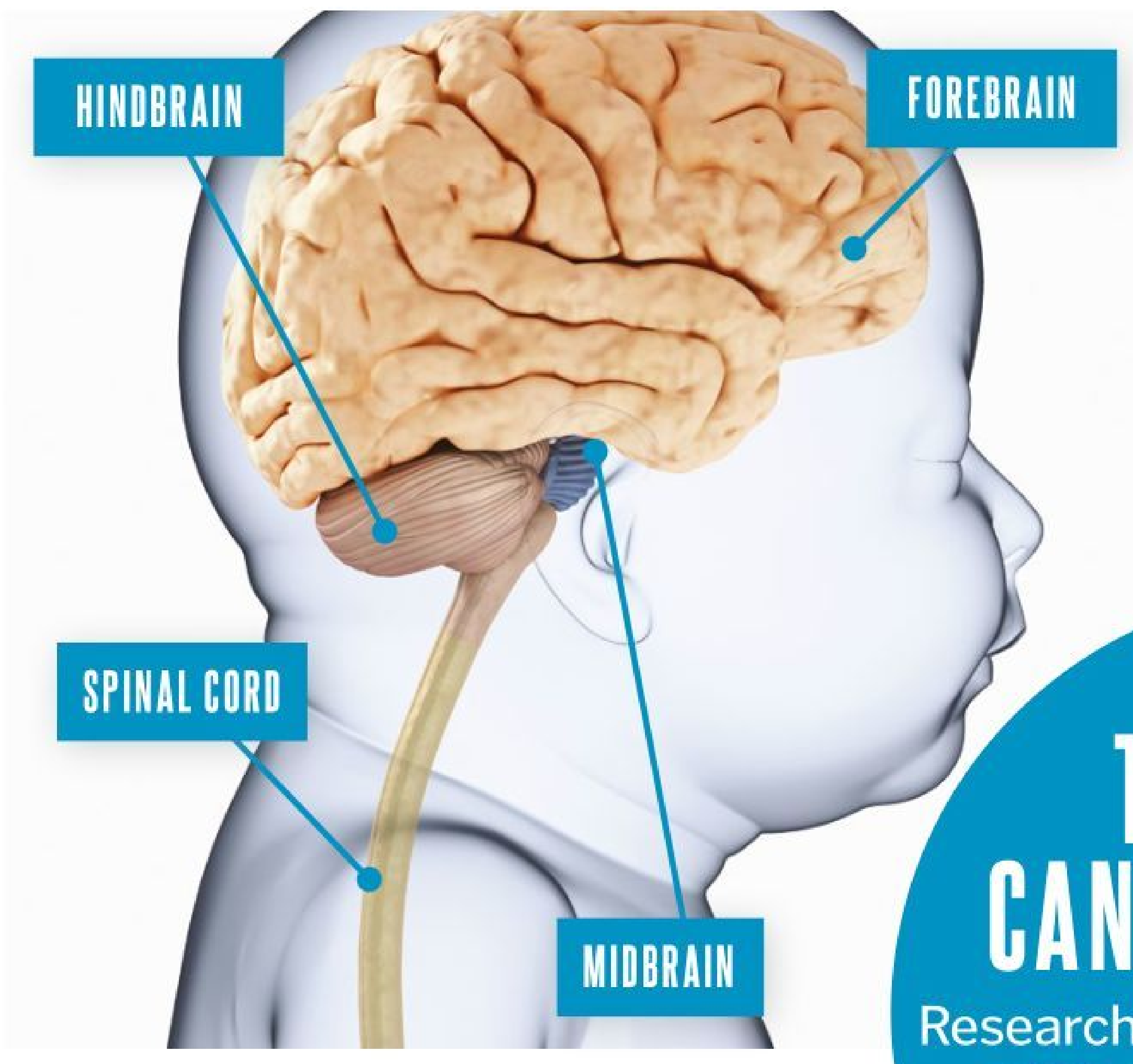
6 WEEKS

The pattern of the brain and spinal cord is now laid out and is gradually refined, controlled by gradients of signalling molecules that assign different areas for different functions.



11 WEEKS

As the embryo becomes larger, the brain continues to increase in size and neurons migrate and organise. The surface of the brain gradually begins to fold. At this point a foetus only measures about five centimetres in length.



BIRTH

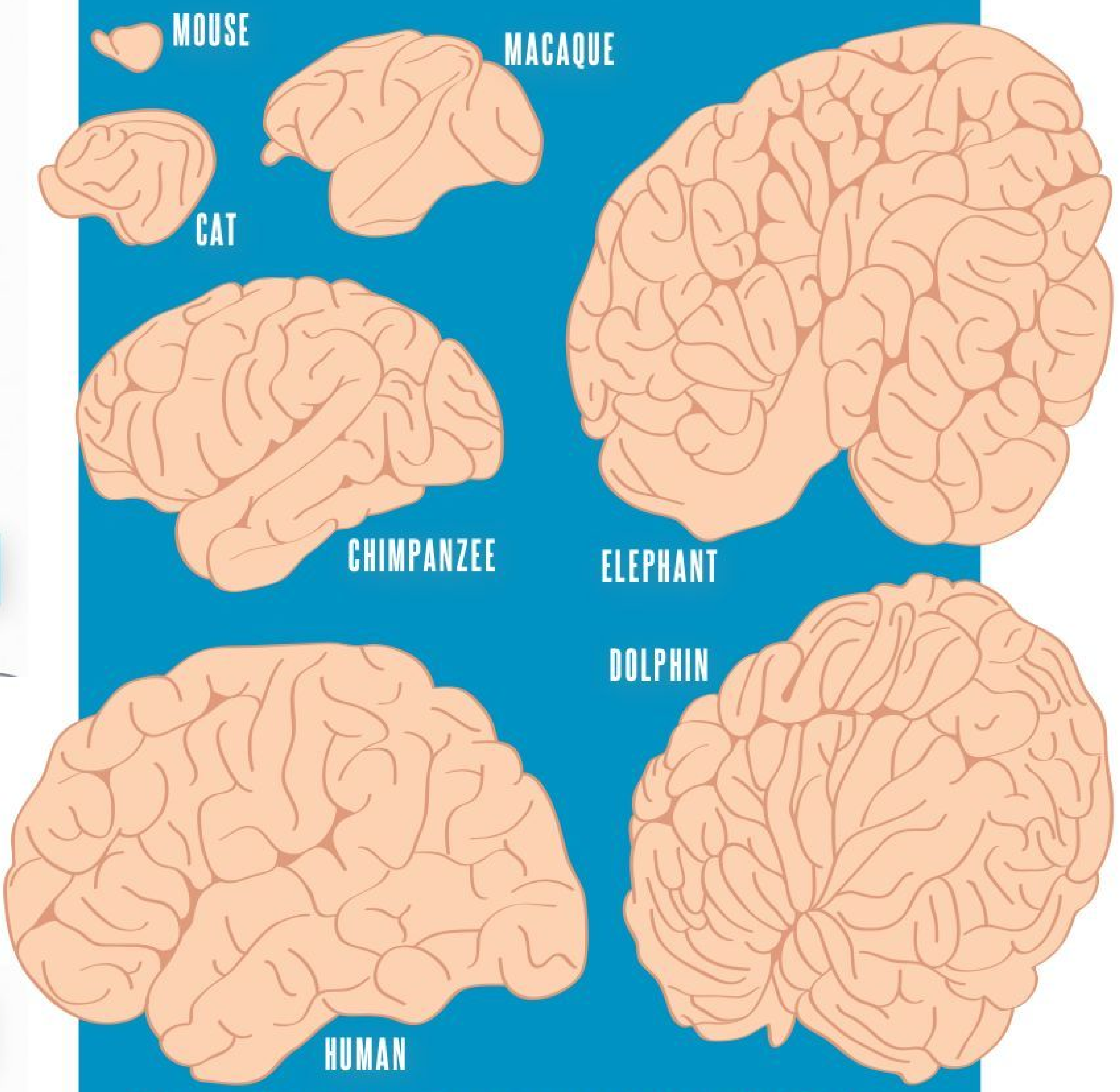
Before a baby is born, around half of the nerve cells in the brain are lost and connections are pruned, leaving only the most useful. This process continues after birth.

WHY THE BRAIN IS WRINKLED

THE BRAIN FOLDS IN ON ITSELF TO CRAM IN MORE PROCESSING POWER

The folds and pockets of our brains are a biological rarity that we only share with a few other species, including dolphins, some primates and elephants. It's a clever evolutionary adaptation that allows intelligent species to squash a huge amount of cortical tissue into a small space, allowing enormous brainpower to be crammed into our relatively small skulls.

Folding starts during the second trimester of pregnancy, creating ridges (gyri) and fissures (sulci), but the biology behind the distinctive wrinkles is stranger than you might think. The organisation of the brain is determined by complex cascades of chemical signals, but the overall shape seems to be the result of simple physics. Grey matter sits on the outside of the brain and, during development, its growth rapidly outpaces the growth of white matter underneath. This puts mechanical stress on the structure, forcing the outside to buckle and curl.



More wrinkled brains are associated with higher intelligence (brain sizes not to scale)

THE BRAIN CAN REGENERATE

Research has shown that certain areas of the adult brain can continue to produce new neurons, a process known as neurogenesis.

> *"Our brains contain 86 billion neurons and 180,000 kilometres of fibres"*

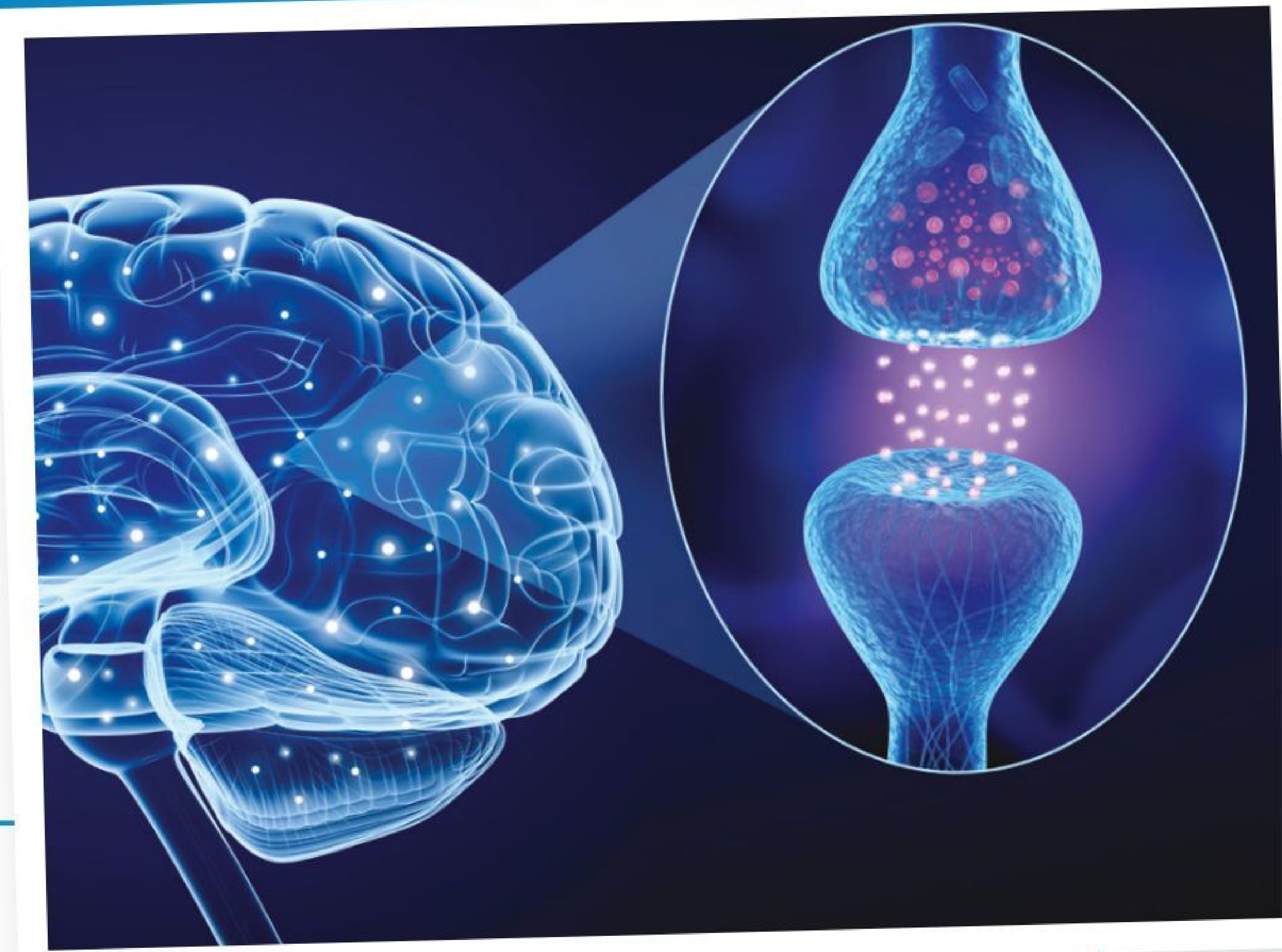
MAKING MEMORIES

THE BRAIN CAN STORE AROUND 1 MILLION GIGABYTES OF DATA

A team at the Salk Institute in California estimate that the brain can store around 1 petabyte of information, stuffed into the connections between nerve cells. That's around 2,000 years' worth of MP3 music or 223,000 DVDs. And, incredibly, it's possible to watch memories being made.

The Weizmann Institute in Israel and UCLA in the US captured memory formation in action. Patients watched clips of videos and were then asked to recall what they had seen. The neurons that lit up in their brains when they watched the clips the first time then lit up again as they relived the experience inside their heads – a bit like an echo.

Recent research from the US and Japan has suggested that these echoes are actually stored twice – once in the hippocampus and again in the cortex. The hippocampus handles short-term storage and gradually forgets, but as it does so it helps to reinforce the memory in the cortex, allowing for long-term recall.



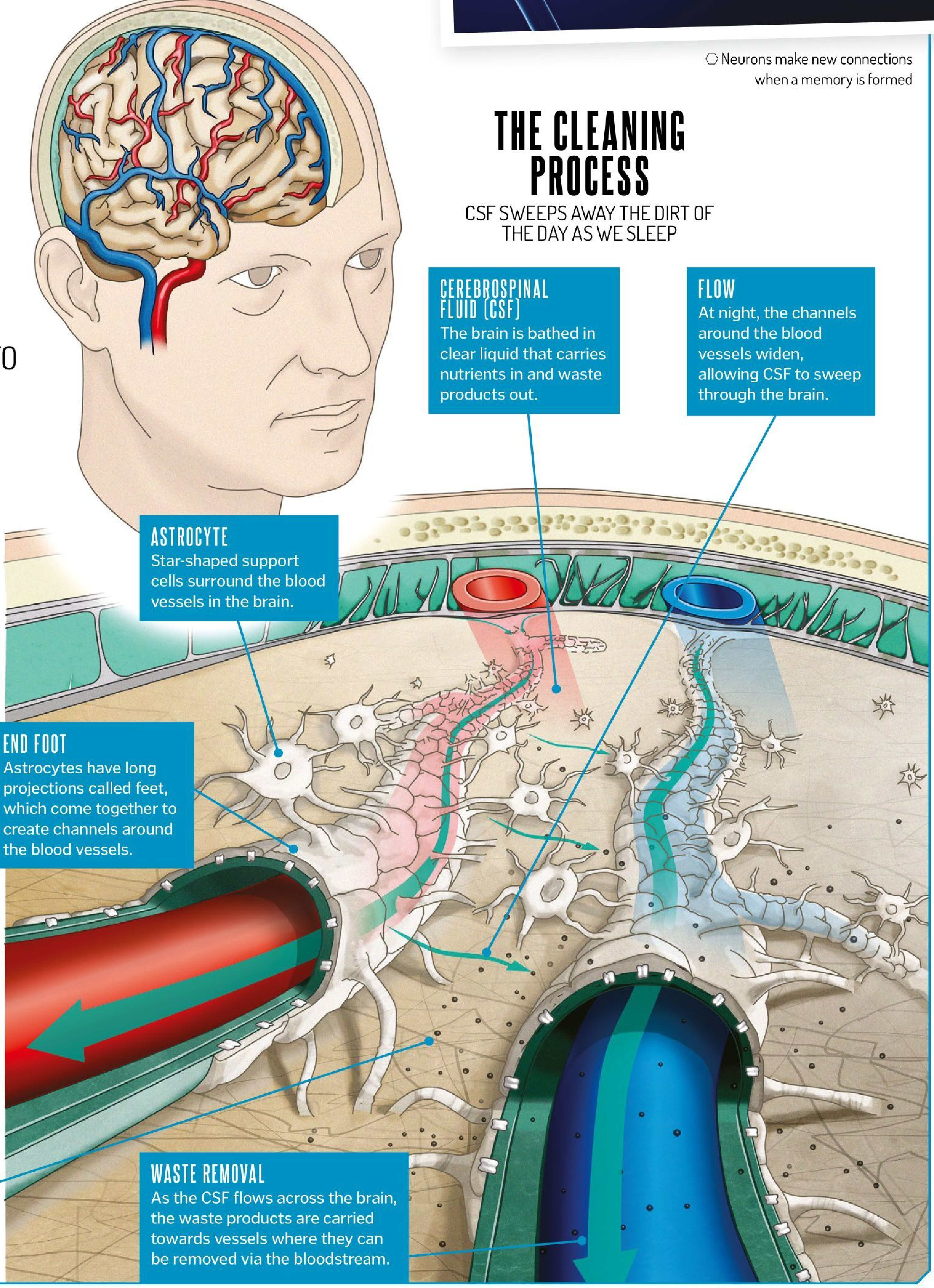
Neurons make new connections when a memory is formed

SELF-CLEANING BRAINS

WE HAVE A BUILT-IN SYSTEM TO CLEAR TOXIC WASTE FROM BETWEEN OUR BRAIN CELLS

Sleep is one of the brain's great mysteries, but research on mice has revealed an intriguing night-time cleanup system. The brain is shielded by a barrier made and maintained by cells called astrocytes. They hug the blood vessels, controlling what's allowed in and out, and a space between the vessel wall and these cells seems to play a crucial role in keeping the brain clean.

At night, the astrocytes relax their grip and the space fills up with a clear liquid called cerebrospinal fluid (CSF). It's pushed along by the movement of the blood vessels underneath, swishing up through the astrocytes and out into the spaces between brain cells. As it passes it picks up waste and debris, carrying the particles back towards the bloodstream so that they can be removed from the brain.



THE CLEANING PROCESS

CSF SWEEPS AWAY THE DIRT OF THE DAY AS WE SLEEP

CEREBROSPINAL FLUID (CSF)
The brain is bathed in clear liquid that carries nutrients in and waste products out.

FLOW
At night, the channels around the blood vessels widen, allowing CSF to sweep through the brain.

ASTROCYTE
Star-shaped support cells surround the blood vessels in the brain.

END FOOT
Astrocytes have long projections called feet, which come together to create channels around the blood vessels.

WASTE
Brain cells are constantly creating waste products that can cause damage if they're allowed to build up.

WASTE REMOVAL
As the CSF flows across the brain, the waste products are carried towards vessels where they can be removed via the bloodstream.

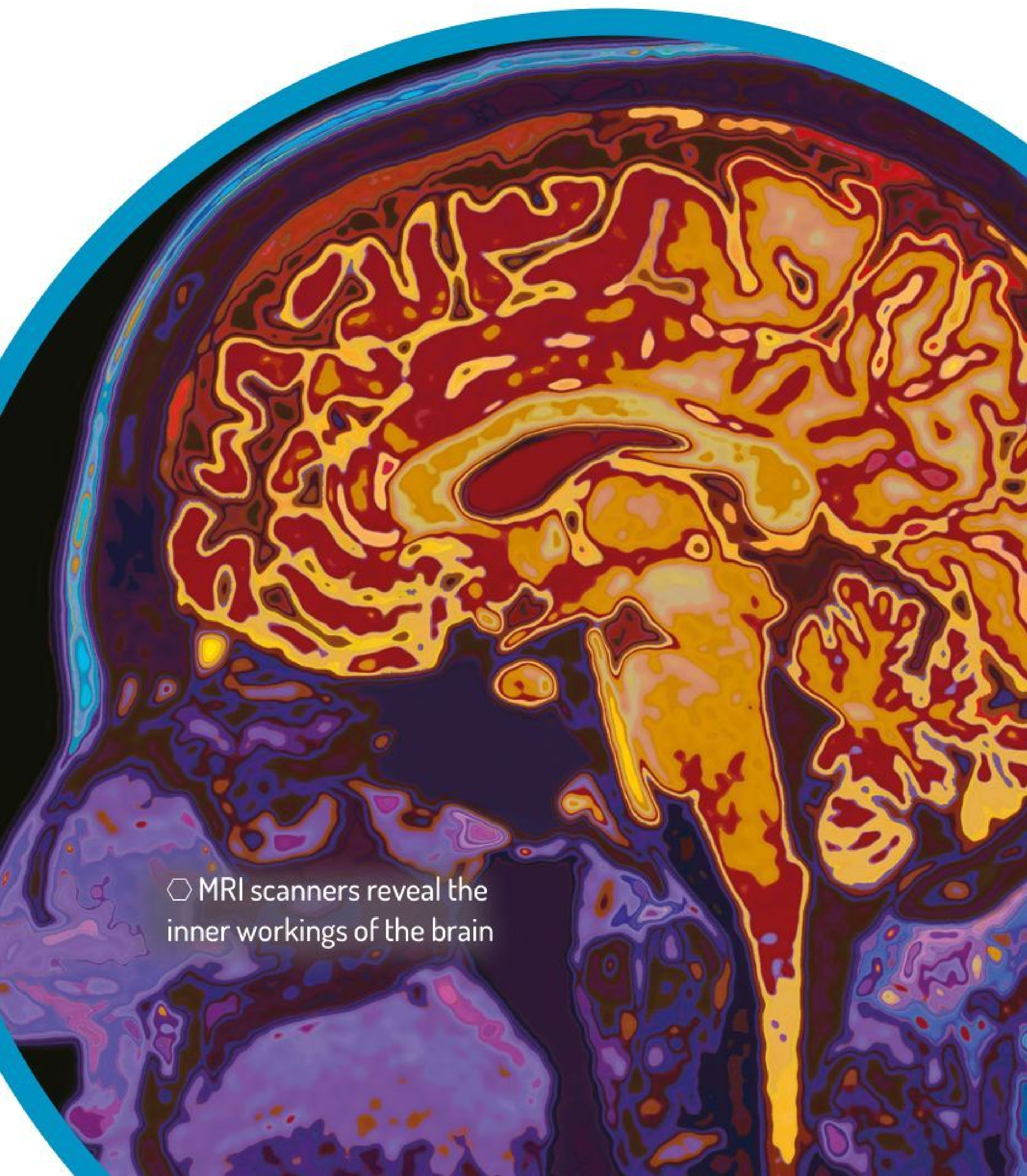
Electrodes can detect the electrical signals produced by our brains

MIND READING

THOUGHTS ARE ELECTRICITY, AND THAT MEANS THAT THEY CAN BE DETECTED AND DECODED

Electrodes placed on the scalp can listen out for signals made by the buzzing of neurons inside the brain, and researchers are developing ways to decode the messages. It works by using a computer that can learn the patterns that the brain creates when people focus on a single, simple thought, like a movement or a word. The signals can then be used to control a prosthetic, command a computer, or they can even be sent to someone else's brain using magnets placed across their scalp.

It might sound like science fiction, but this field is moving so quickly that even big companies like Facebook want in on the action. In 2017, Mark Zuckerberg announced that the company is "working on a system that will let you type straight from your brain about five-times faster than you can type on your phone". They're also working on a skin sensor that can translate touch into thoughts, mimicking what the ear does with sound.



MRI scanners reveal the inner workings of the brain

MIND OVER MATTER

SHEER BRAINPOWER DRIVES THE HEALING IMPACT OF THE PLACEBO EFFECT

Placebos are an important part of testing new treatments. Before new medicines or procedures hit the clinic, they are compared to a pill, patch or injection that doesn't contain any active ingredients. Neither the doctor nor the patient know which is which, helping to prevent bias. But the brain is a powerful thing, and just thinking you're getting treatment can make you feel better – or give you side-effects.

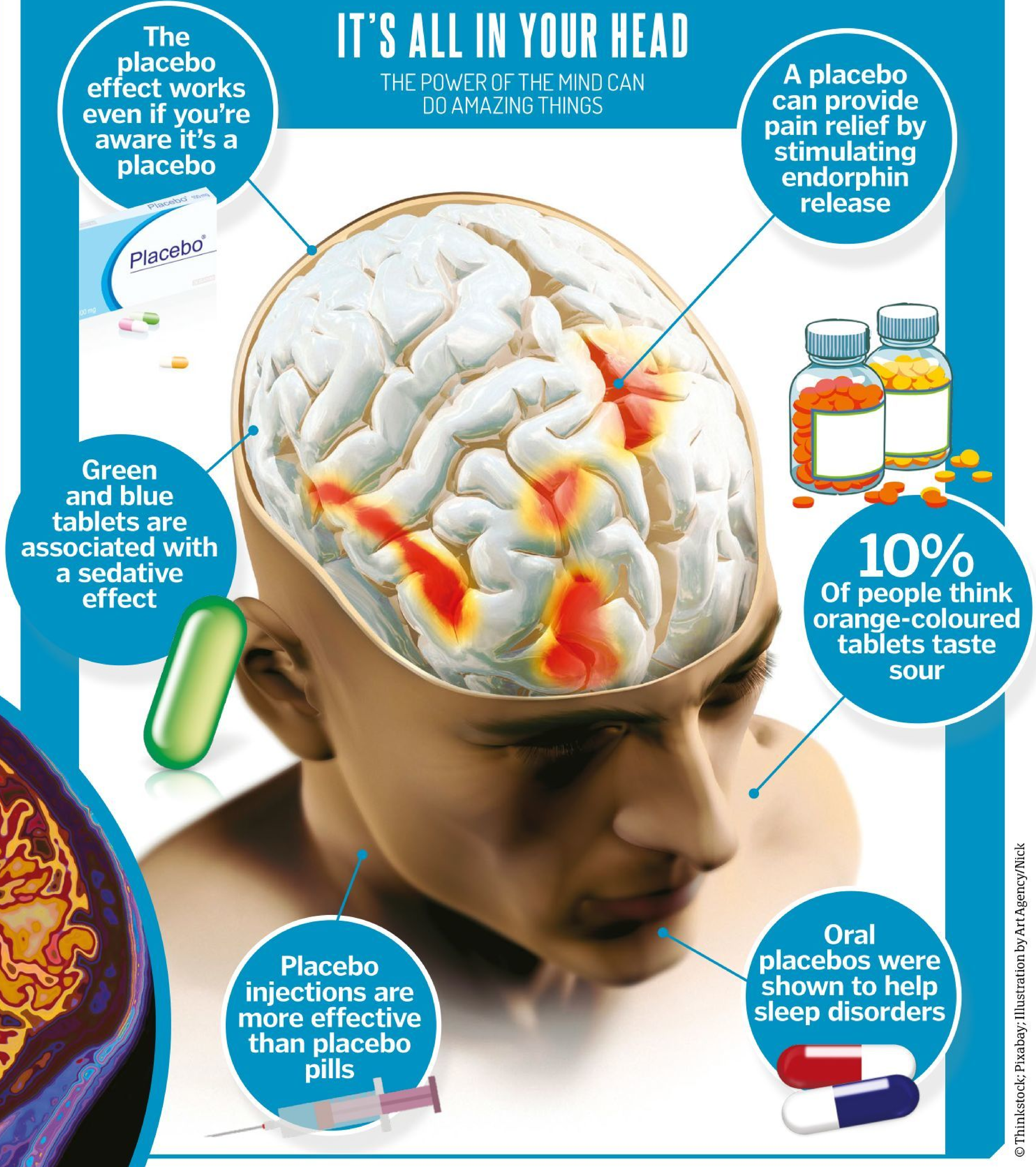
One of the most famous studies, led by American neuroscientist Jon Levine in 1978, attempted to find out what was happening. He and his team gave placebo 'painkillers' to patients after wisdom tooth extraction. Their studies revealed that the pain relief the patients experienced was actually down to the release of their own natural painkillers – endorphins.

This strange effect can't cure cancer or get rid of asthma, but, with a little help from sugar pills and saline injections, your brain can change the way you feel.

> "Just thinking you're getting treatment can actually make you feel better"

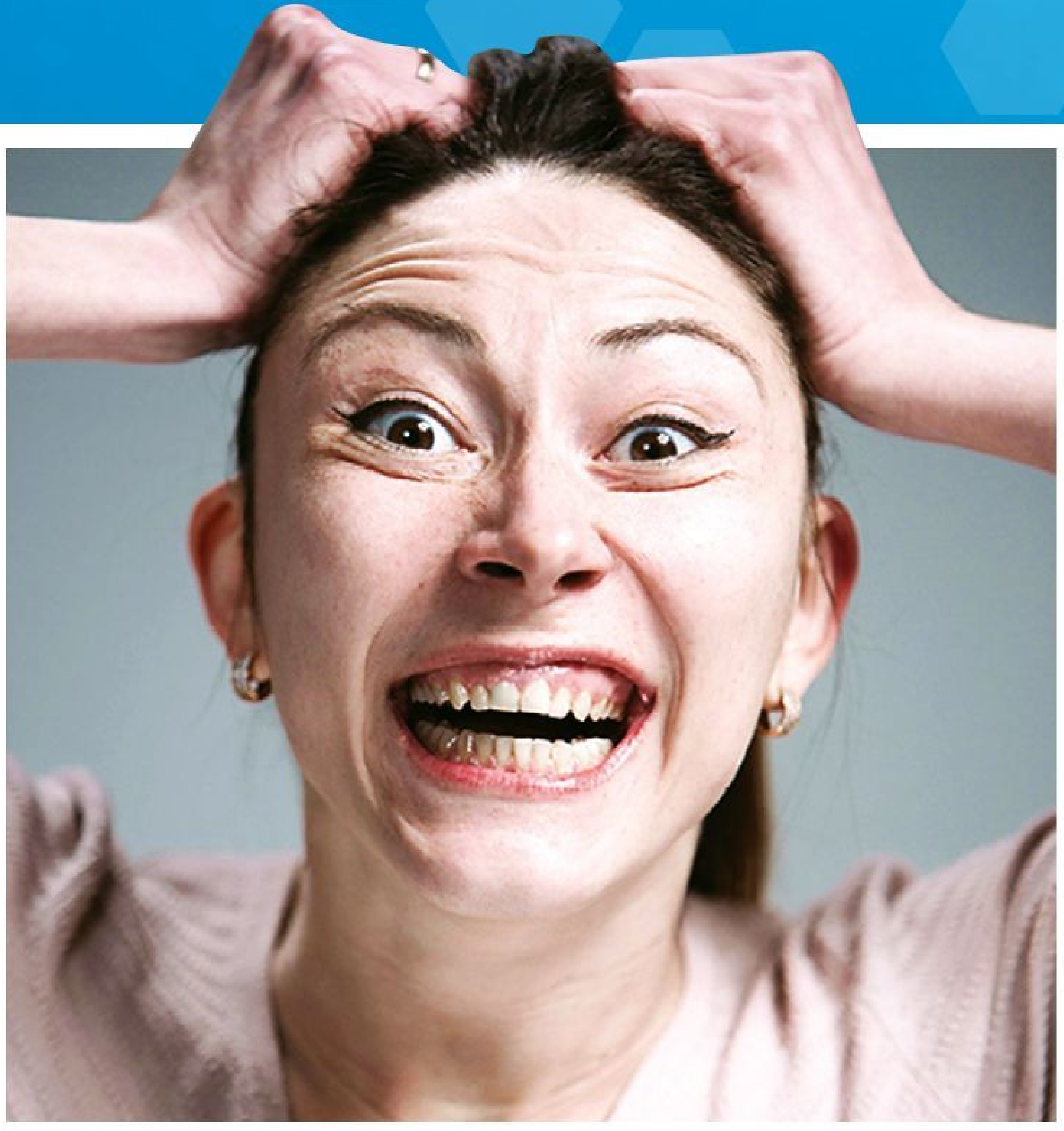
IT'S ALL IN YOUR HEAD

THE POWER OF THE MIND CAN DO AMAZING THINGS



The placebo effect works even if you're aware it's a placebo
A placebo can provide pain relief by stimulating endorphin release
Placebo
Green and blue tablets are associated with a sedative effect
10% Of people think orange-coloured tablets taste sour
Placebo injections are more effective than placebo pills
Oral placebos were shown to help sleep disorders

© Thinkstock; Pixabay; Illustration by Art Agency/Nick

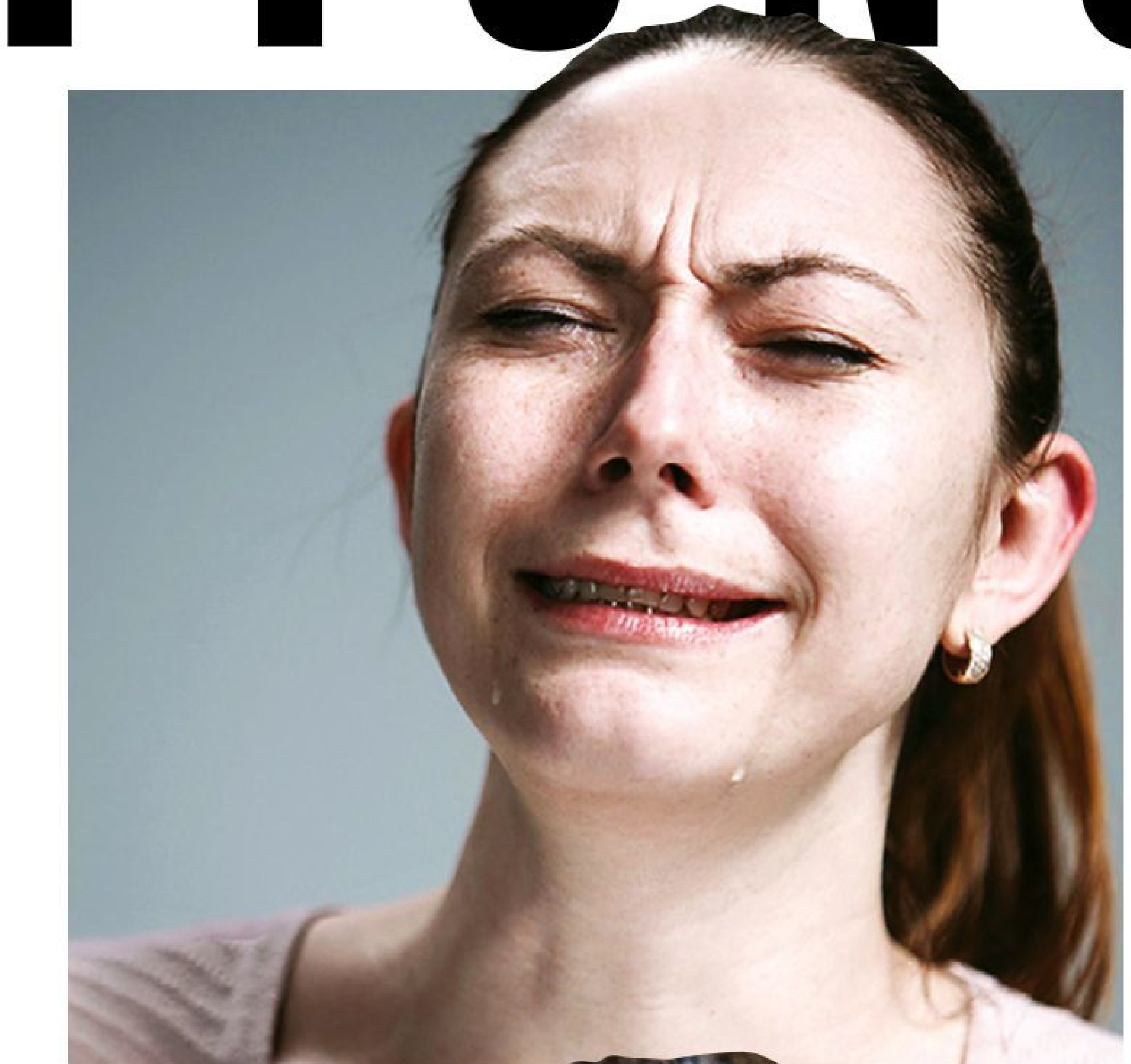


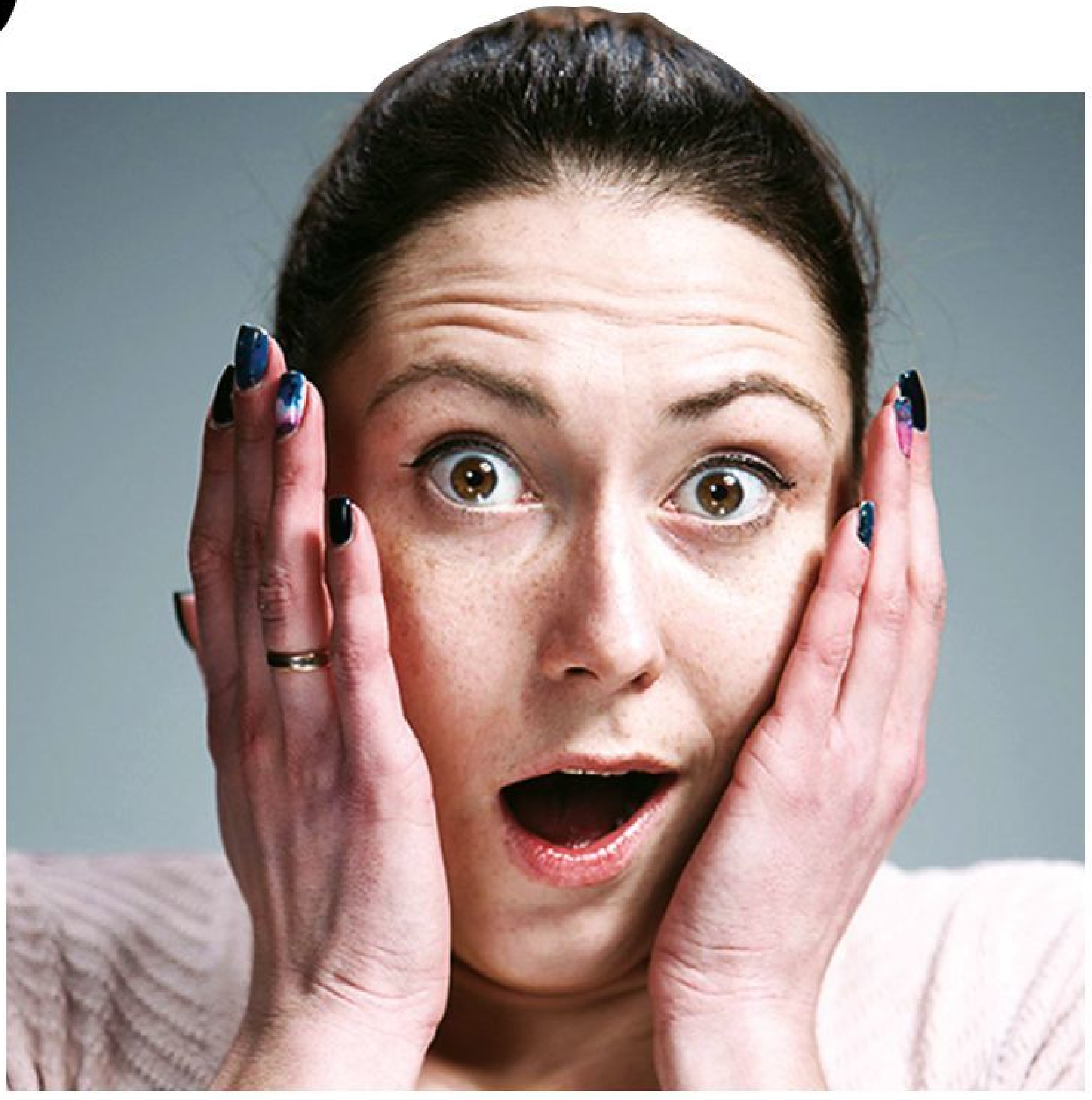
THE SCIENCE OF EMOTIONS

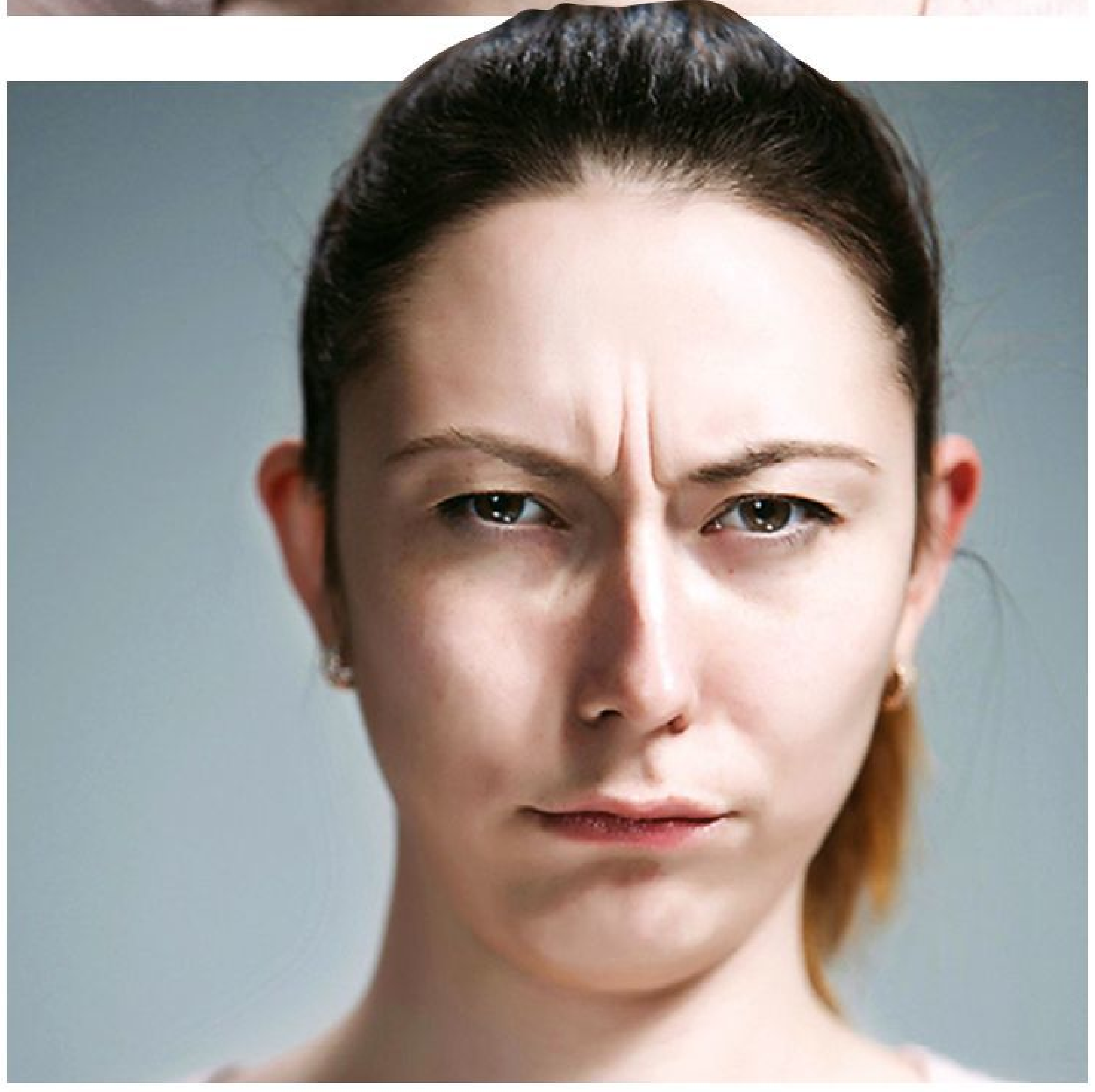
HOW OUR ANCIENT BRAINS EVOLVED THE PERFECT WAY TO KEEP US SAFE BY CONTROLLING THE CHEMICALS IN OUR MINDS TO MODERATE OUR BEHAVIOUR

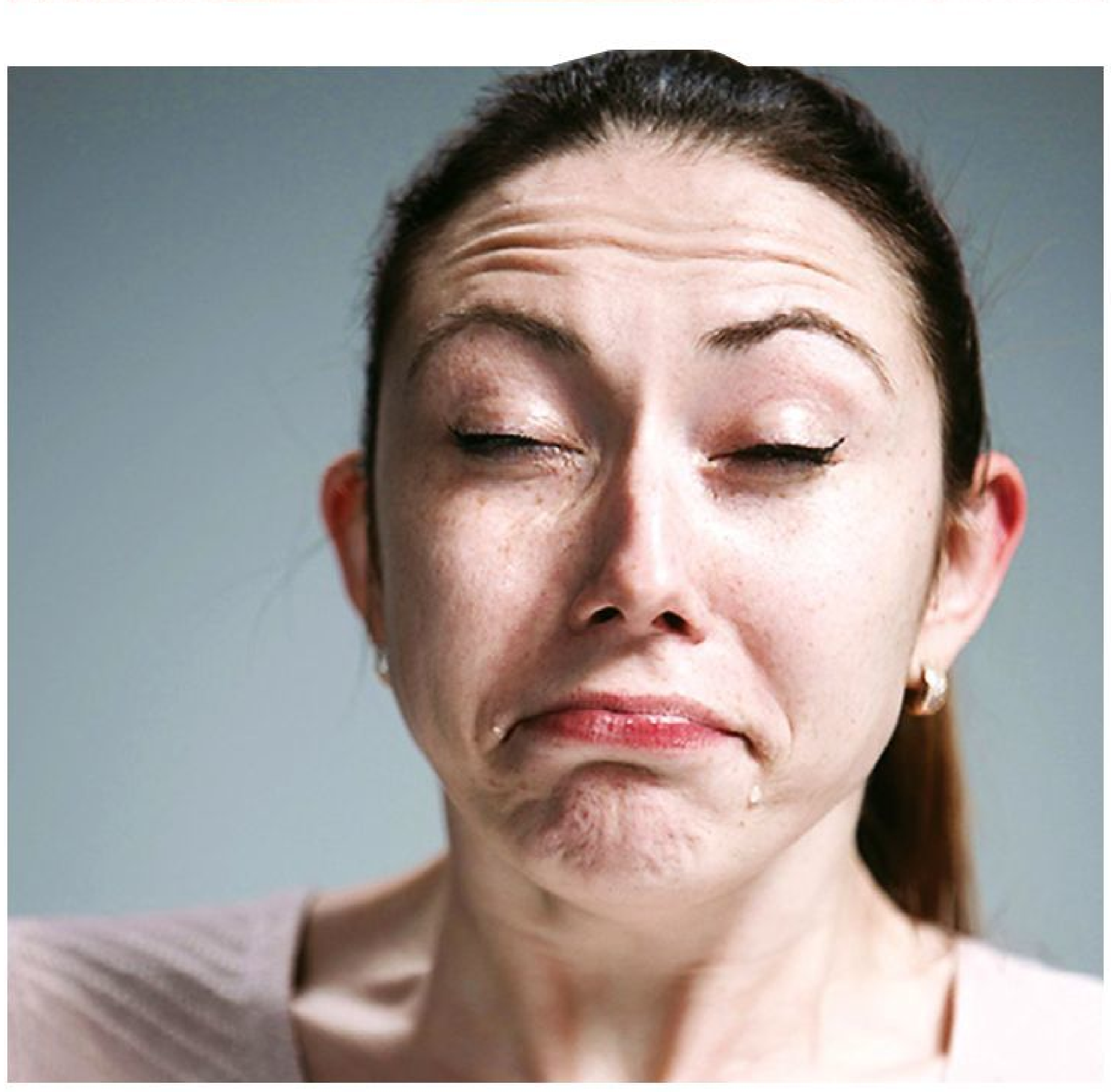
How are you feeling right now? Are you relaxed laying on your sofa and listening to the gentle sounds of the dawn chorus outside your window? Or maybe you are tense with your shoulders hunched up around yourself as you try to get five minutes peace in a busy office? You would think that it is easy to work out if we are happy or sad, angry or calm, but humans cycle through such a vast array of emotions throughout their lives it can be difficult to distinguish them from one another.

Emotions are not a simple experience. Every time you feel something your body initiates a physiological change, a chemical release and a behavioural response. This process involves multiple processes working together, including your major organs, neurotransmitters and limbic system. Your limbic system is the most









primordial part of your brain, thought to have first evolved in early mammals. It's filled with ancient neural pathways that activate our emotions in response to stimuli and controls our fight-or-flight response through the autonomic nervous system.

This response evolved from a need to make decisions based on our emotions. As our body fills with adrenaline and our heart starts racing we prepare to react. Do we stay to fight the bear that has come scavenging for food, or do we flee to somewhere safe? We can still feel the effects of this response. When we are confronted for not doing the dishes we might feel the same fight-or-flight response as our adrenaline starts to flood our system. Our heart rate and breathing increases, the fine hairs on our arms might stand on end, and our hands feel clammy as we decide whether we are going to stay and argue or if we are going to escape to the sanctuary of our bedroom.

The biological sensations in our bodies in response to emotions can feel very similar to one another. Imagine your palms sweating, feeling your cheeks warm as they flush red, and your heart pounding in your chest. You could feel this because you are sitting nervously in the dentist's waiting room, or you could be excited as you wait to see your loved ones after they return from a holiday – the physiological reaction is the same. The interpretation of emotions is our logical brain rationalising these responses and describing them as feelings. We take into consideration the context and label our emotions accordingly. However, we don't all do this the same way. Because our bodies cause different floods of chemicals in response to different environmental triggers, each person naturally reacts to situations differently.

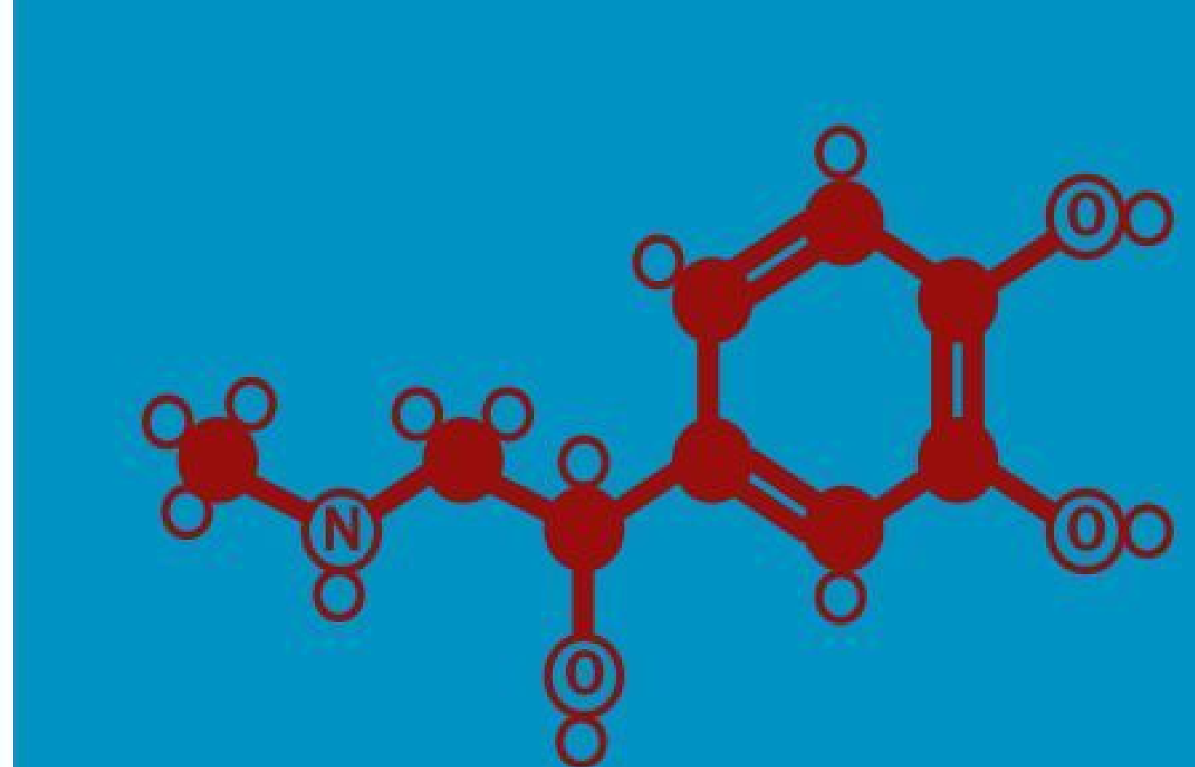
Have you ever seen someone who is being berated in a meeting but facing the onslaught with nothing more than a slightly raised eyebrow? Or watched as someone finds out some bad news but keeps their composure? You are sure that you would have raised your voice or burst into tears, but our responses are defined by how our neurons are networked together. Our past experiences and genetic predispositions influence our brain chemistry and therefore our physiological responses,

> *"We feel our emotions, and not just in our head and heart – our bodily state changes to react to the chemical storm in our system"*

THE CHEMISTRY OF EMOTIONS

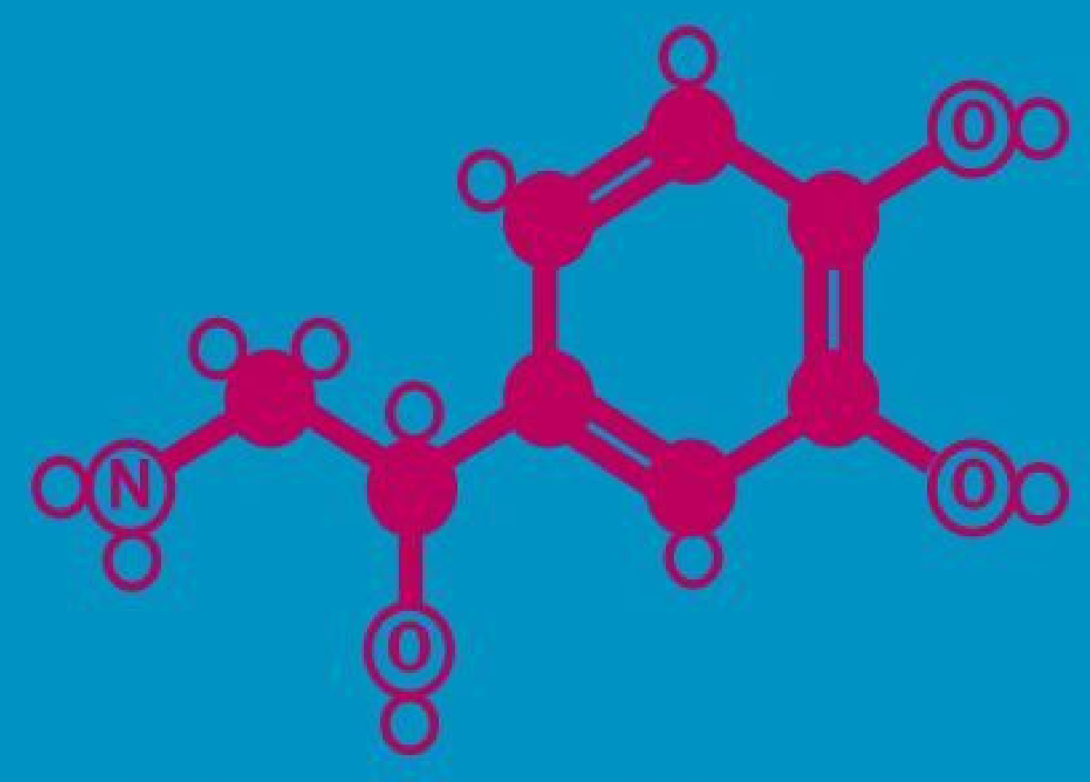
Where two neurons meet, a very small gap (synapse) exists between them. The electrical impulse travelling along the axon of the neuron must convert into a chemical signal to bridge this gap. The chemicals that do this are called neurotransmitters. These so-called chemical messengers are involved in our different responses to situations.

Your emotions depend on fluctuating levels of neurotransmitters, which cause the activation of different parts of the brain responsible for different moods, or activate parts of the brain that trigger the stimulation of the autonomic nervous system.



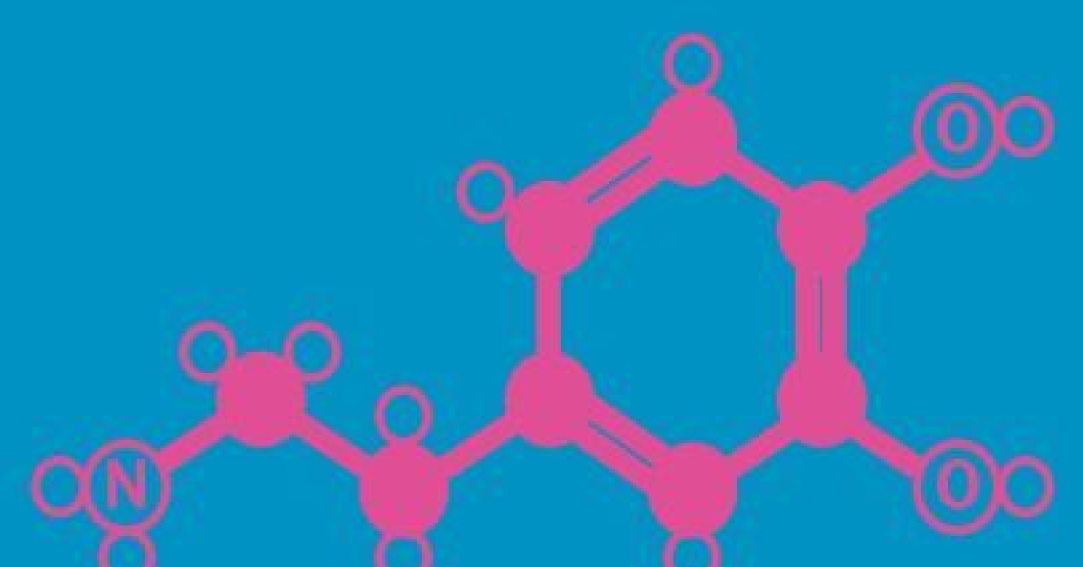
ADRENALINE

Released by the adrenal glands that sit on top of each kidney, adrenaline increases the flow of blood to our muscles, raises our heart rate and dilates our pupils. It is crucial in our fight-or-flight survival response.



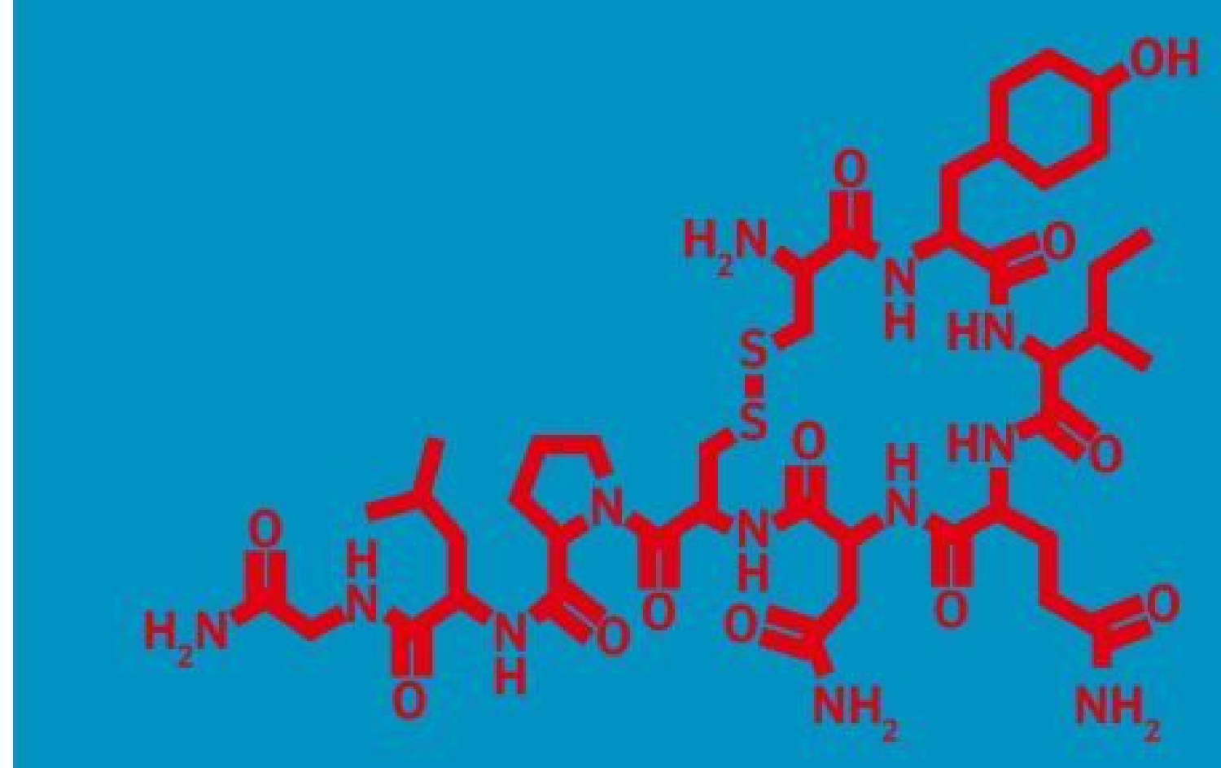
NORADRENALINE

Similar to adrenaline, the release of this chemical can result in increased levels of alertness, helping to prime us for action if needed. It also increases our blood pressure and widens our air passages.



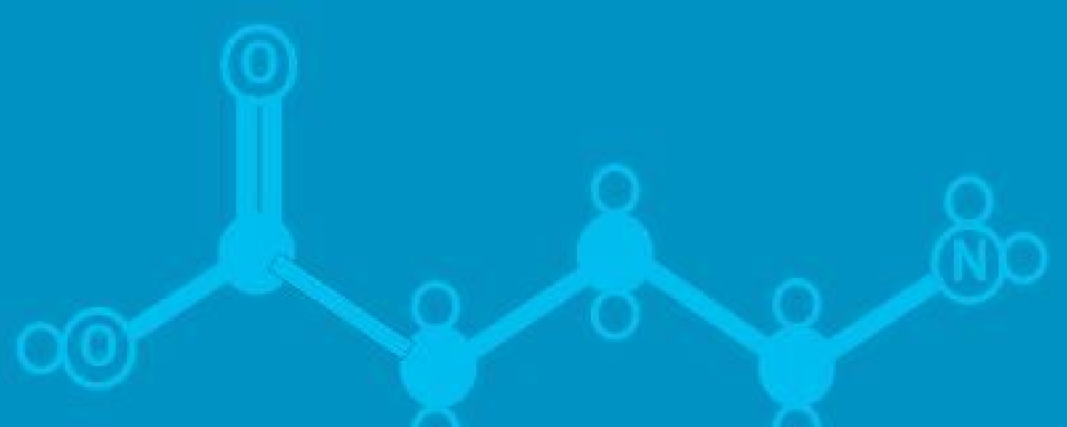
DOPAMINE

This is the addictive reward chemical that your brain craves. It serves to motivate you to seek out the things you need for your survival. We can sometimes find ourselves enslaved by this ancient reward mechanism.



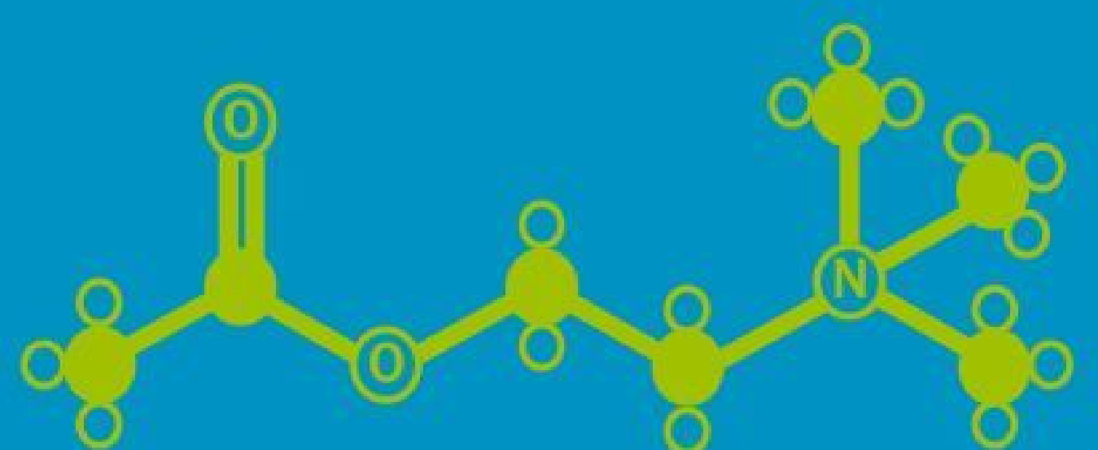
OXYTOCIN

Also known as the 'cuddle hormone', oxytocin is released when you're close to another person. It's essential for making strong social bonds, and it's also a key part of why we want to trust people.



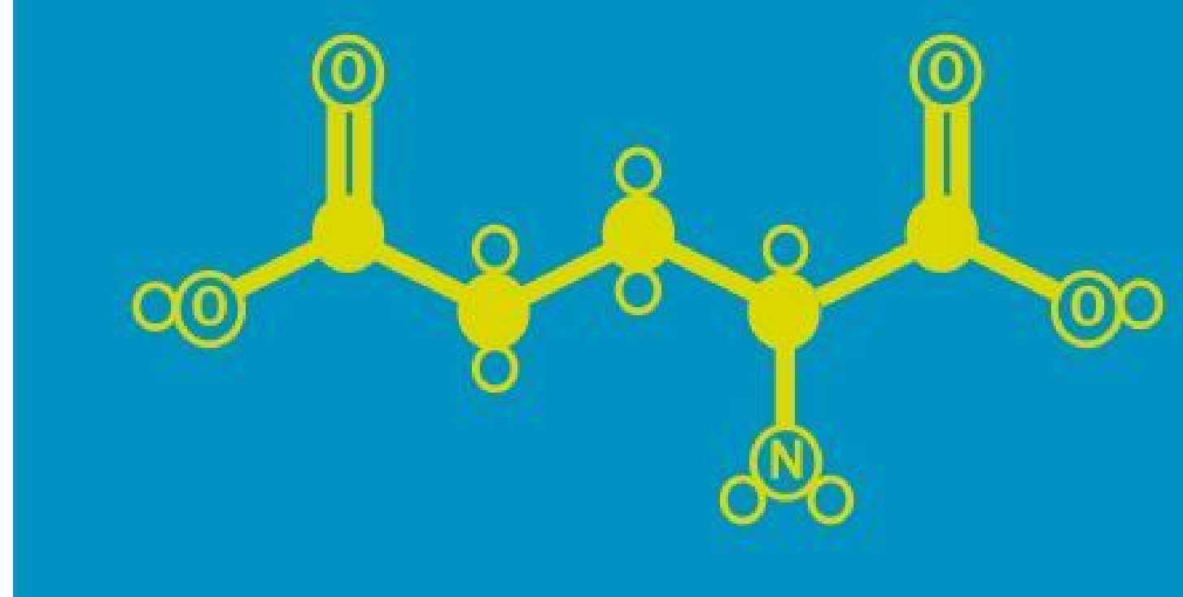
GABA

Responsible for regulating muscle tone, gamma-Aminobutyric acid (GABA) also regulates the communication between brain cells. It can calm us down by reducing the rate at which our neurons fire.



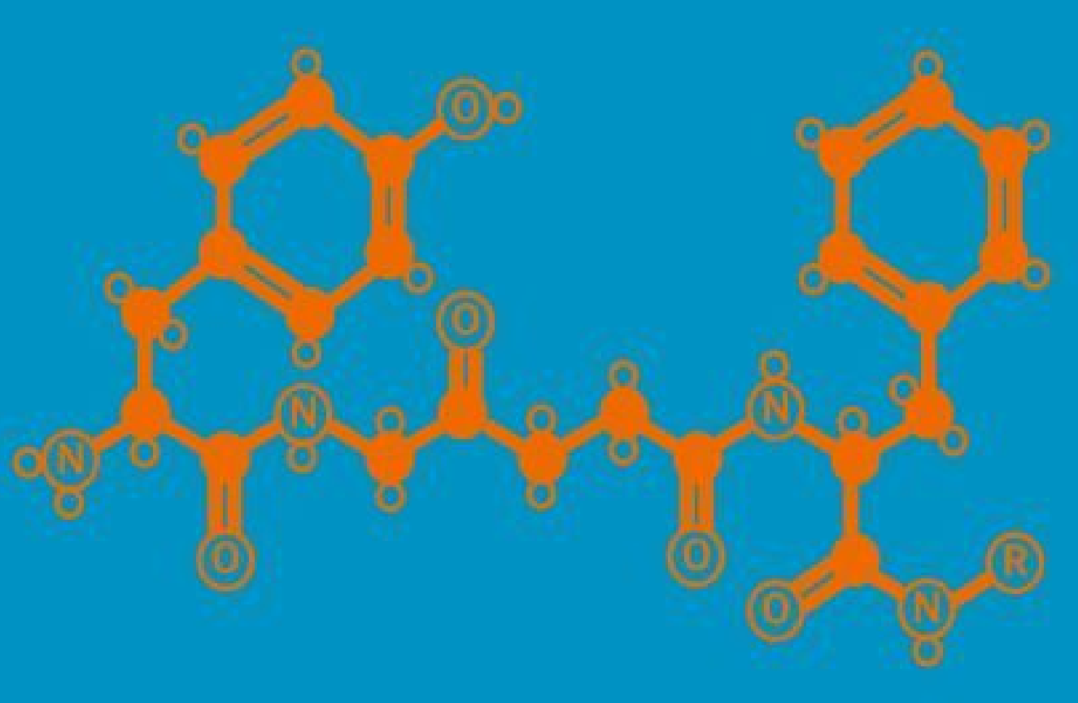
ACETYLCHOLINE

This is the main neurotransmitter in the parasympathetic nervous system that slows our heart rate, contracts smooth muscles, dilates blood vessels and increases bodily secretions.



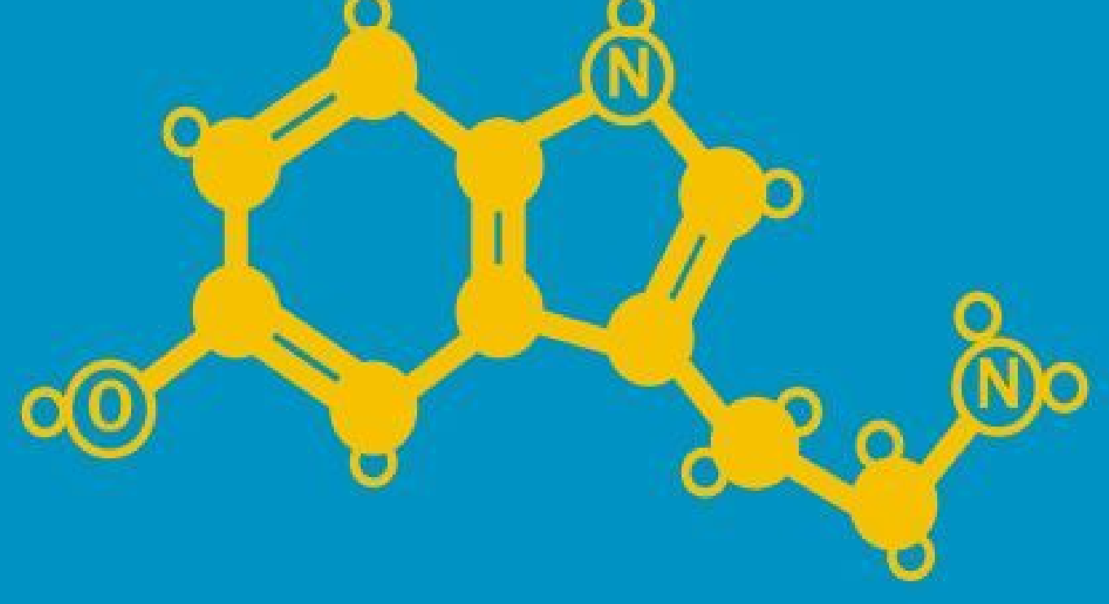
GLUTAMATE

The most abundant neurotransmitter in the vertebrate nervous system, glutamate is used by nerve cells to transmit signals to other cells. Too much of it can cause cognitive impairments.



ENDORPHINS

Triggered by the sensation of pain, endorphins work to inhibit the transmission of pain signals. Capable of producing a sense of euphoria, studies have suggested endorphins may also be stimulated by laughter.

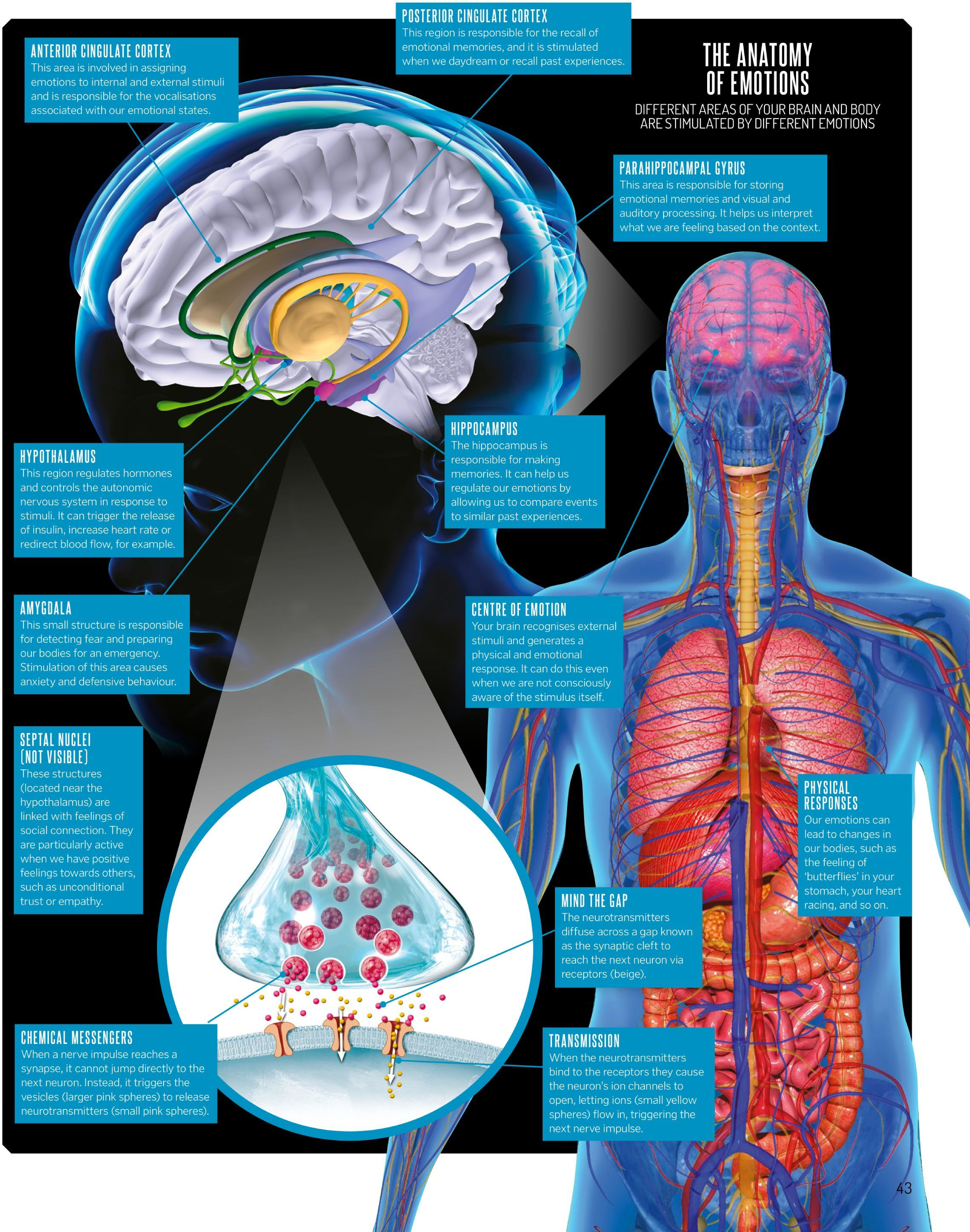


SEROTONIN

Serotonin is linked to our wellbeing and happiness, and our levels of it are affected by sunlight. It also helps to regulate our mood balance, sleep cycle and digestion.

THE ANATOMY OF EMOTIONS

DIFFERENT AREAS OF YOUR BRAIN AND BODY ARE STIMULATED BY DIFFERENT EMOTIONS



ANTERIOR CINGULATE CORTEX
This area is involved in assigning emotions to internal and external stimuli and is responsible for the vocalisations associated with our emotional states.

POSTERIOR CINGULATE CORTEX
This region is responsible for the recall of emotional memories, and it is stimulated when we daydream or recall past experiences.

PARAHIPPOCAMPAL GYRUS
This area is responsible for storing emotional memories and visual and auditory processing. It helps us interpret what we are feeling based on the context.

HYPOTHALAMUS
This region regulates hormones and controls the autonomic nervous system in response to stimuli. It can trigger the release of insulin, increase heart rate or redirect blood flow, for example.

HIPPOCAMPUS
The hippocampus is responsible for making memories. It can help us regulate our emotions by allowing us to compare events to similar past experiences.

AMYGDALA
This small structure is responsible for detecting fear and preparing our bodies for an emergency. Stimulation of this area causes anxiety and defensive behaviour.

CENTRE OF EMOTION
Your brain recognises external stimuli and generates a physical and emotional response. It can do this even when we are not consciously aware of the stimulus itself.

SEPTAL NUCLEI (NOT VISIBLE)
These structures (located near the hypothalamus) are linked with feelings of social connection. They are particularly active when we have positive feelings towards others, such as unconditional trust or empathy.

PHYSICAL RESPONSES
Our emotions can lead to changes in our bodies, such as the feeling of 'butterflies' in your stomach, your heart racing, and so on.

MIND THE GAP
The neurotransmitters diffuse across a gap known as the synaptic cleft to reach the next neuron via receptors (beige).

CHEMICAL MESSENGERS
When a nerve impulse reaches a synapse, it cannot jump directly to the next neuron. Instead, it triggers the vesicles (larger pink spheres) to release neurotransmitters (small pink spheres).

TRANSMISSION
When the neurotransmitters bind to the receptors they cause the neuron's ion channels to open, letting ions (small yellow spheres) flow in, triggering the next nerve impulse.

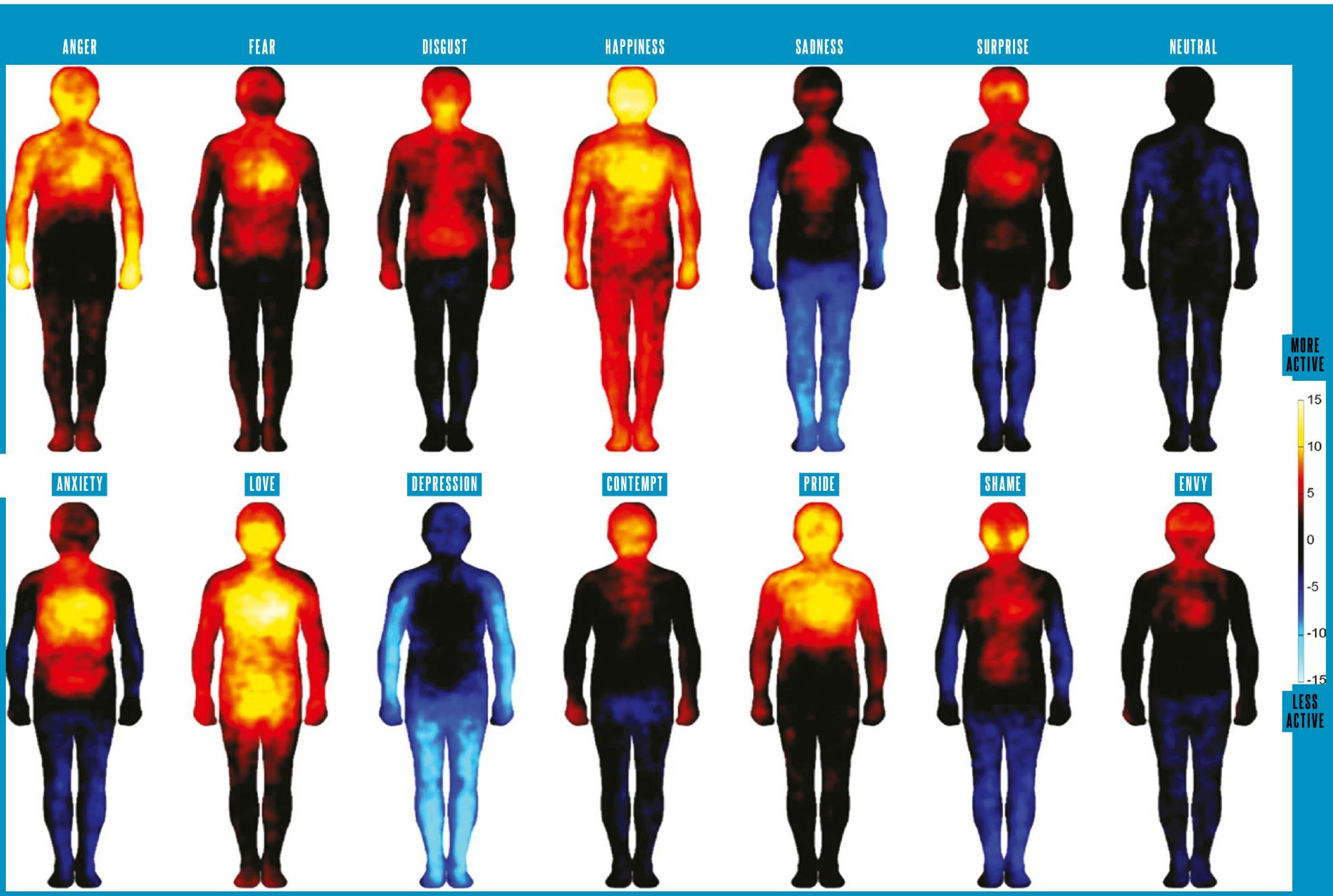
○ The chemicals released when we're close to our family help us to build trust and closeness

which in turn determine how we react to various situations – like someone cancelling on us last minute, or having a friend surprise us by showing up at the front door unannounced.

At times our emotions can seem like an irrational response, but our brains have carefully evolved these mechanisms with just one target – keeping us alive. While we interpret different emotions as positive or negative, the most ancient parts of the human brain developed them on the principle that we must survive. We evolved emotions as a means of communicative function and to help us navigate social interactions and our environment safely: they are designed to protect us. Our fear responses were originally a survival tactic that warned us of potential dangers, such as our innate unease around spiders and snakes. Then there is the feeling of disgust, which warns us of foods or other substances that may be dangerous.

Our other emotions are responses to social interactions that keep us part of a group. We are fundamentally a social species and throughout our evolution have relied on our tribe to help us survive. Anger is a response to perceived social threats or a signal of dominance, pride can help us to boost our social status, while shame is intended to decrease our standing within a group. These emotions maintain the social balance of our tribe – who we follow, who we trust, who we care about.

The fundamental emotions that motivate us individually are almost always sadness and



EMOTIONS AS SENSATIONS

We feel our emotions, and not just in our head and heart – our bodily state changes to react to the chemical storm in our system. We might feel a tight knot in our stomach as we dread walking onto a stage to give a speech, or we might feel our cheeks flush red when we answer a question wrong.

Researchers from Aalto University in Finland explored how humans physically feel their emotions by mapping the sensations topographically. Their findings were consistent across Western European and East Asian cultures, which suggests the way people feel during an emotional experience stems from a biological source rather than a cultural interpretation. The study also highlighted that emotions adjust our bodily state to either prepare ourselves physically to fight or flee or to encourage us to seek out enjoyable social reactions.

The study included over 700 participants from Finland, Sweden and Taiwan, and researchers induced different emotional states before asking them to colour bodily areas on images of the human body to describe in which areas they felt activity increasing or decreasing.

happiness. Sadness results from loss and serves the biological purpose of motivating a person to recover that loss, whether it is a young child searching for their mother in a supermarket, or trying hard to get a new job after being dismissed. But the ultimate human emotion is happiness, and we are all in search of it.

When you're sitting around a campfire, safe in the countryside with some close friends and good food, you feel happiness because you have found the resources that your primitive brain is seeking. Our species is drawn so much to happiness because this emotion is our brain's reward system for finding environments where we are free from threat. A healthy human brain copes with sadness when social bonds are broken, communicates with our loved ones and can recognise and regulate our emotions even when they do not feel particularly positive.

The next time you sit in an airport departure lounge, look for the emotions. Our bodies have created these experiences – the tears as we say goodbye, the smiles as we are reunited – for the purpose of keeping us alive. Our emotions and feelings are what make us human, but it means we're in for a bit of a rollercoaster along the way.

The emotional mechanisms in our bodies evolved to keep us safe and connect us with others

> *"Reading the emotions of others is a vital skill for navigating our way through life"*

UNIVERSAL EXPRESSIONS

Reading the emotions of others is a vital skill for navigating our way through life – it would be awkward to misunderstand your friend as happy when they're actually angry with you.

There has been a long-established view that the way we express our feelings using our facial expressions is universal and crosses all cultures for seven basic emotions: anger, disgust, fear, joy, sadness, surprise and contempt. For over a century, studies have explored the theory of universal expression by asking people to interpret photographs displaying various emotions, although there are some cultures around the world that do not have the same perception of certain emotions.

One study found that people living in the Trobriand Islands off Papua New Guinea didn't interpret images of people who were wide-eyed with their lips parted as they gasped as a sign of fear. Instead, the Trobrianders interpreted this emotion as anger. This research is some of the first to suggest that how we express our emotions is not universal and may differ between societies.

While the expression of happiness and sadness is generally the same all over the world, surprise and fear can be interpreted differently between cultures

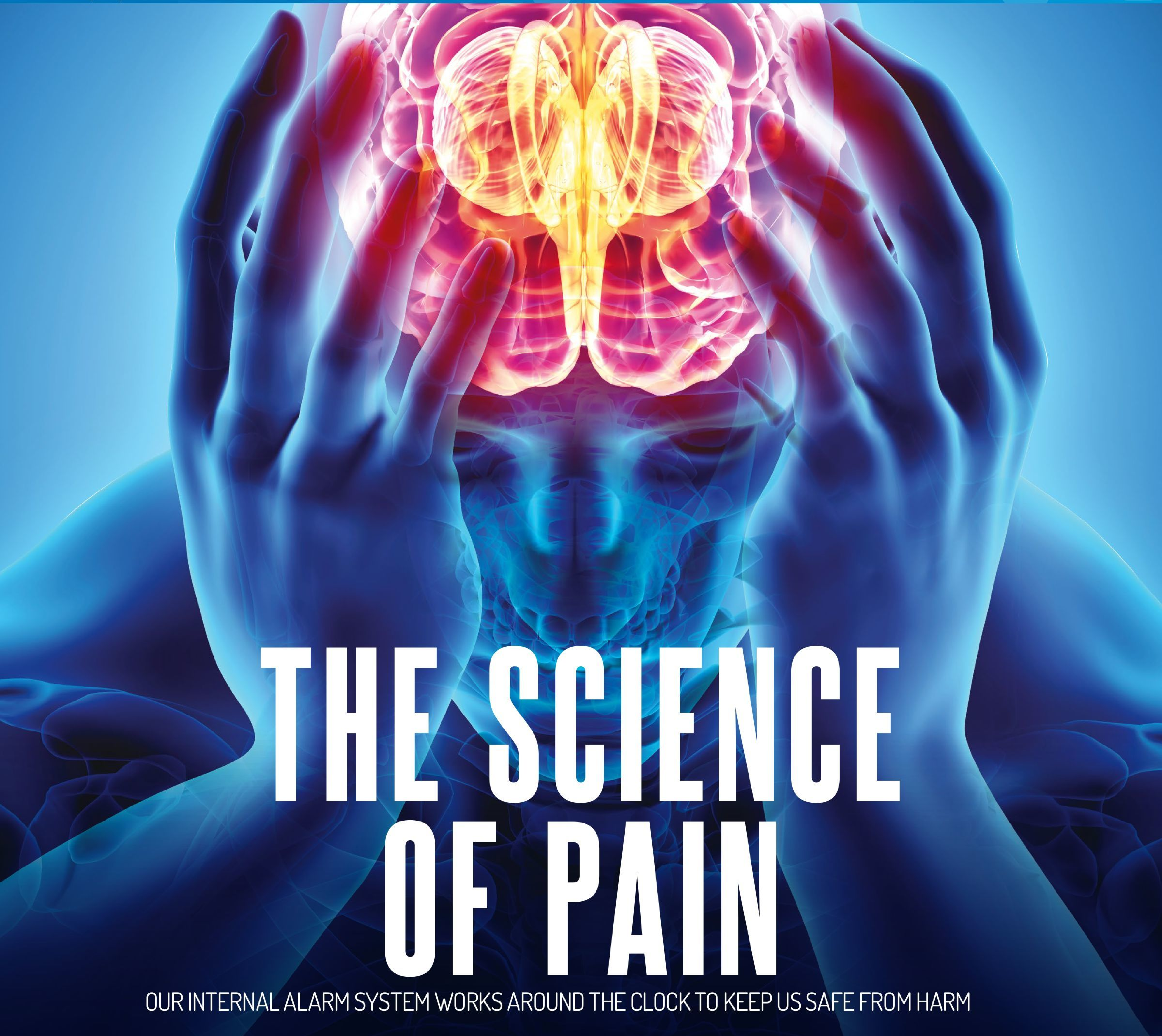
HOW MANY EMOTIONS DO WE HAVE?

It has long been thought that there are only six different emotions: anger, disgust, fear, happiness, sadness and surprise. It has been hypothesised that any other emotions are just a combination of these basic feelings, such as anticipation being caused by a mixture of fear and happiness. However, a recent study published in *Proceedings of the National Academy of Sciences of the United States of America* from researchers at UC Berkeley suggests that we may have many more emotions that are distinctively different to one another but still related.

The study used 2,185 short videos with the intent to evoke emotions in the 853 participants. Clips included a cute baby playing with some fluffy puppies, a man holding a tarantula inside his mouth and a happy couple getting married. Participants were asked to record how the videos made them feel and how strongly it evoked a response. The study suggests that there are 27 distinct emotions, including awe, awkwardness, calmness, confusion, disgust, nostalgia, sadness, sympathy, horror and triumph.

We may have more emotions than we are able to express in our languages

© Getty; L Nummenmaa et al, Aalto University



THE SCIENCE OF PAIN

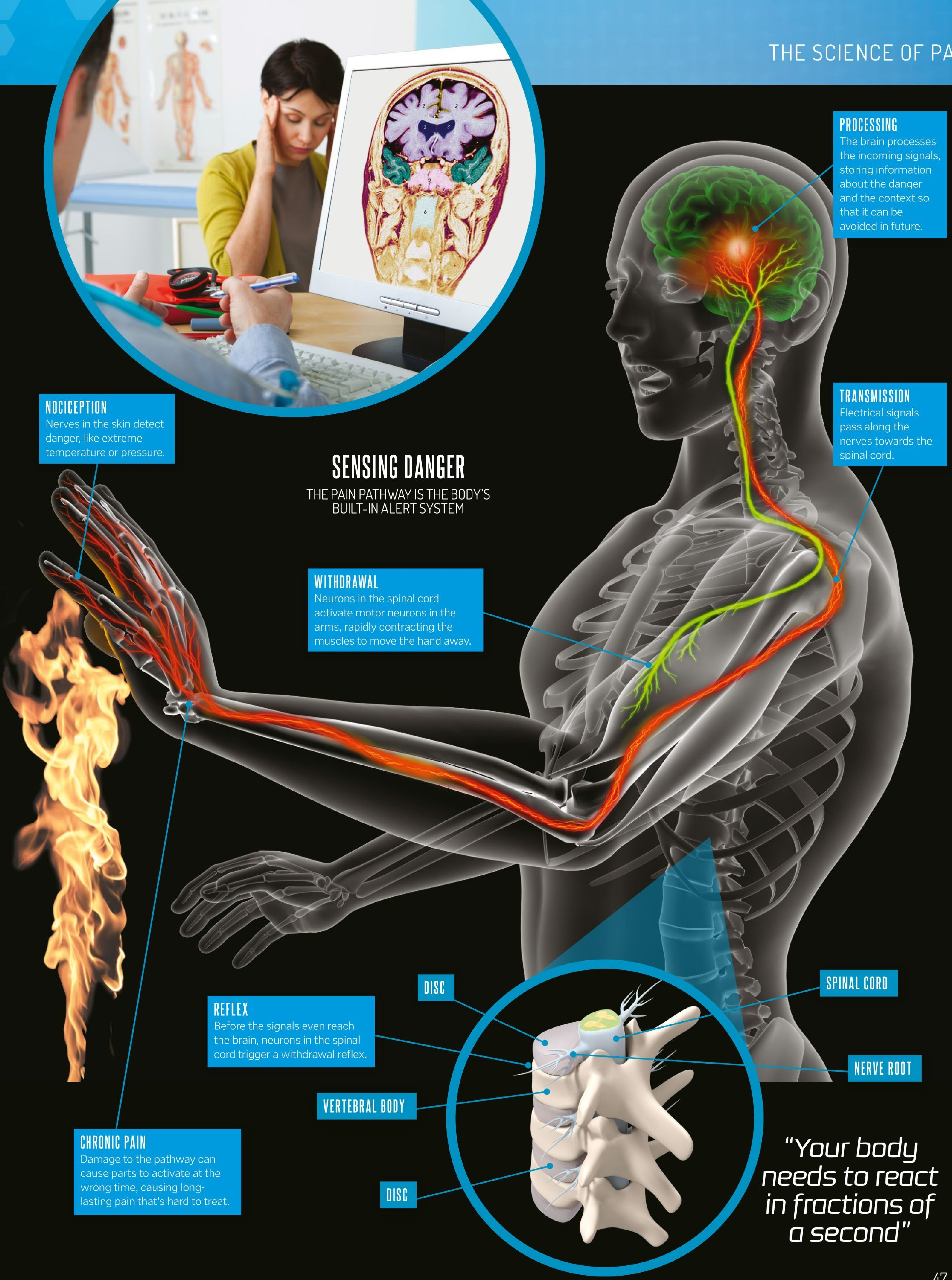
OUR INTERNAL ALARM SYSTEM WORKS AROUND THE CLOCK TO KEEP US SAFE FROM HARM

Millions of sensitive nerves guard our tissues, listening for physical danger. These pain sensors, or nociceptors, are designed to detect temperature, pressure and chemical signals. They have a high threshold for activation and only send messages when the body is at risk of harm.

If skin temperature rises above 40 degrees Celsius or dips below 15 degrees Celsius, thermal nociceptors start to fire. If pressure exceeds three kilograms per centimetre squared, or if the skin stretches or tears, mechano-nociceptors kick into action. And if cells become damaged and start leaking their contents, chemical nociceptors switch on.

A rapid response to nociceptor activation is crucial. If you put your hand in a flame, your body needs to react in fractions of a second. Nociceptors send their signals to the spinal cord, which manages the first step of the response. It can process some of the information without the brain, triggering a rapid withdrawal reflex. This is the very simplest form of damage control, and even primitive animals sense and respond to harm in this way. But pain is more than just a reflex.

As the hand pulls away from the fire, the signal from the nociceptors passes up the spinal cord towards the brainstem. In the brain it enters the cerebral cortex, responsible for cognition and consciousness. Processing here ties the incoming sensory signals to memory and emotion, producing the complex feeling of pain. The unpleasant experience that follows helps us to remember harmful activities and to avoid them in the future.



SENSING DANGER

THE PAIN PATHWAY IS THE BODY'S BUILT-IN ALERT SYSTEM

NOCICEPTION
Nerves in the skin detect danger, like extreme temperature or pressure.

PROCESSING
The brain processes the incoming signals, storing information about the danger and the context so that it can be avoided in future.

TRANSMISSION
Electrical signals pass along the nerves towards the spinal cord.

WITHDRAWAL
Neurons in the spinal cord activate motor neurons in the arms, rapidly contracting the muscles to move the hand away.

REFLEX
Before the signals even reach the brain, neurons in the spinal cord trigger a withdrawal reflex.

CHRONIC PAIN
Damage to the pathway can cause parts to activate at the wrong time, causing long-lasting pain that's hard to treat.

> "Your body needs to react in fractions of a second"

© Getty; Illustration by The Art Agency/Barry Croucher

THE DIFFERENT TYPES OF PAIN

Pain can be short-term (acute) or long-term (chronic). It can be mild, uncomfortable, distressing or debilitating. It can feel achy, dull, raw, sharp, stabbing, throbbing or burning. It might be constant or it might come and go. But beneath these different experiences, all pain falls into two main categories: nociceptive and neuropathic.

Nociceptive pain is the normal response to tissue damage. Pain nerves sense extreme temperature, extreme pressure or harmful chemicals and they send signals to the brain. This alerts us to danger, encourages us to rest the injured area and reminds us to avoid the situation in the future.

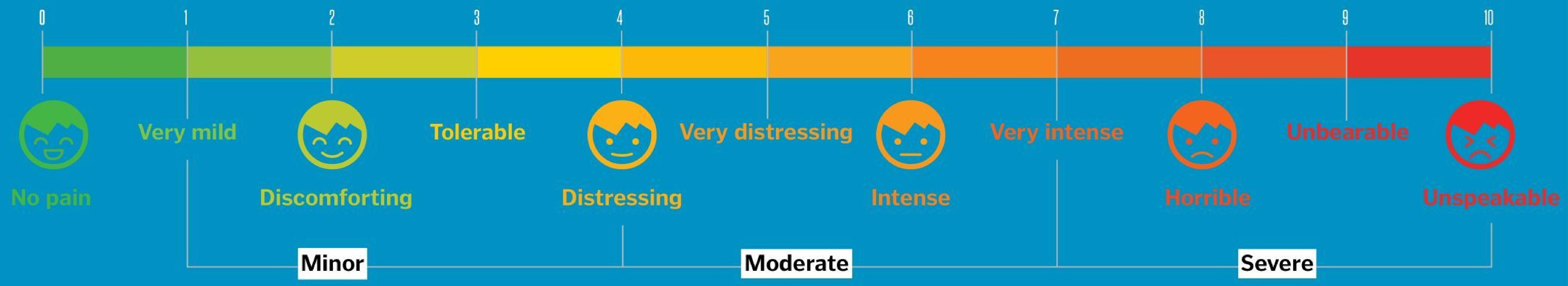
Neuropathic pain, by contrast, does not serve a useful purpose. It is the result of nerve damage. Certain injuries, illnesses and infections harm pain-sensing neurons, and if the body cannot make repairs, they can start to misfire. The nerves send pain signals when there shouldn't be any pain, and the brain can't tell the difference. This type of pain is particularly challenging to treat.

○ The arthritic joints in the hand on the right cause nociceptive pain

CAN WE MEASURE PAIN?

How do you convert the subjective experience of pain into cold hard numbers? One of the first attempts was to use a dolorimeter, a device that would push or burn the skin until the patient said 'ouch'. This would reveal their pain threshold; the amount of pressure or heat they could tolerate. Today, the most common measure of pain is simply to ask someone how they're feeling and how much it hurts on a scale of one to ten. However, scientists at the University of Colorado have been using brain scans to make this more scientific.

Using a dolorimeter-like approach, they applied heat to the skin, but instead of waiting for people to say 'ouch', they watched their brains. In total, 114 people took part in the study, which also included scientists from three other US universities. Each person experienced a range of different temperatures, which revealed a signature pattern of brain activity that predicted the level of physical pain they felt. The pattern differed from emotional pain and decreased with painkillers, providing an objective way to see how much something really hurts.



○ Some studies have suggested that women feel pain more intensely

ACUTE VS CHRONIC PAIN

SPOT THE DIFFERENCE BETWEEN THESE TWO MAJOR TYPES OF PAIN

ACUTE		CHRONIC
Resolves after the illness or injury gets better	**TIME**	Continues long after the injury heals
Nerve activation in response to actual tissue damage	**CAUSE**	Not always clear
Alert system to avoid damage and allow time to heal	**PURPOSE**	No clear biological purpose
Focused on tackling the underlying cause of the pain	**TREATMENT**	Focused on managing pain and minimising the impact

© Getty; Science Photo Library

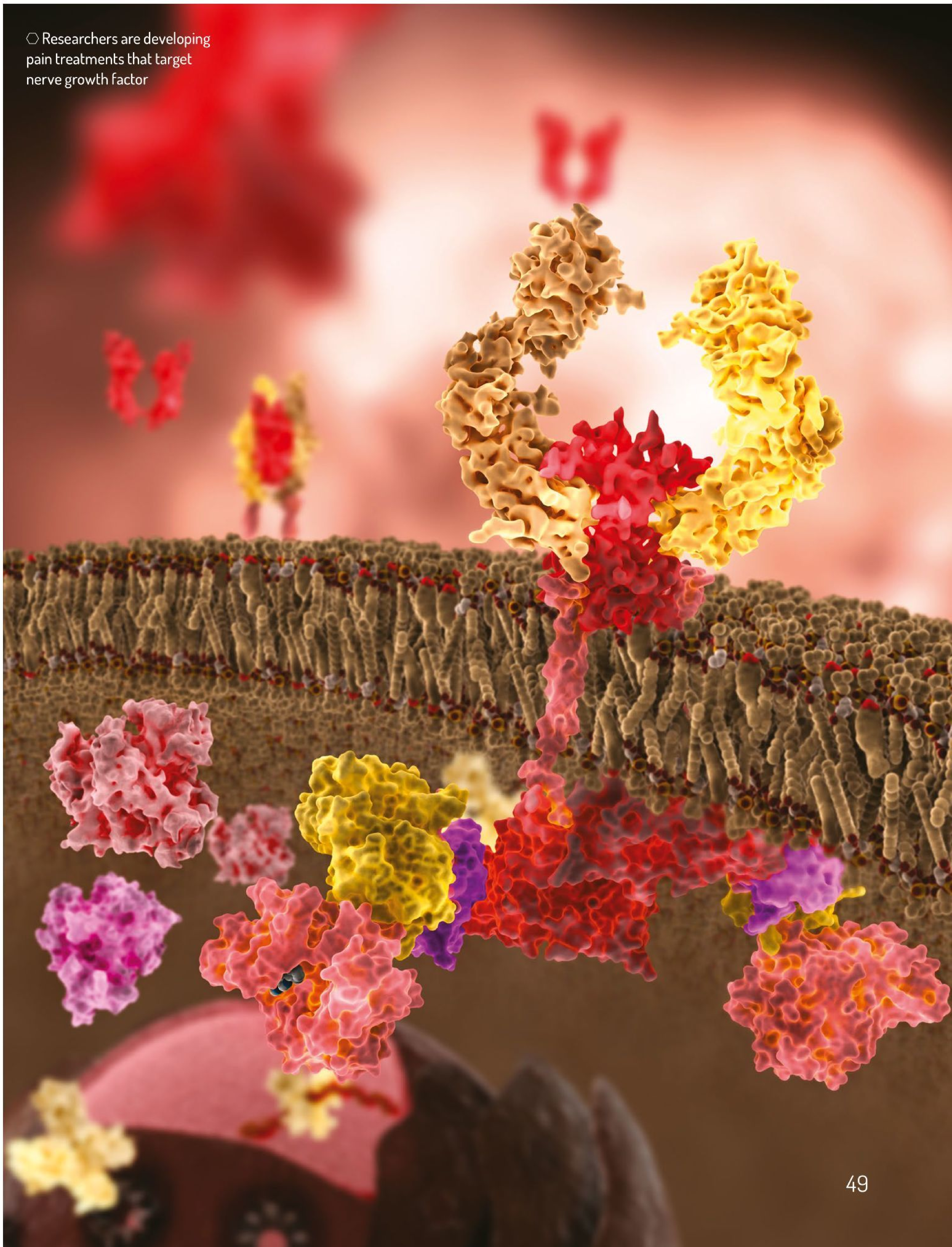
TREATING CHRONIC PAIN

Over-the-counter painkillers tend to target inflammation, which means they are not always particularly useful for chronic pain. Opiate painkillers, like codeine and morphine, can stop pain messages reaching the brain, but they are addictive and their effectiveness decreases over time, so they are not recommended for long-term treatment. Other options include antidepressants and anticonvulsants; these actually change the brain's chemistry, but they don't work for everyone.

The pharmaceutical industry has been looking at a chemical produced by the brain called nerve growth factor (NGF). NGF changes the pain sensitivity of nerves, and blocking its activity in animals has been shown to help to reduce pain, but trials conducted in humans in 2010 had dangerous side-effects, including loss of blood to the bones. There is still a lot of work to do to find out whether they are safe to use.

Physical and psychological therapy can help to provide some distraction, but many people struggle daily with chronic pain. Without a cause for doctors to treat, it can be extremely hard to manage.

> *"Nerve growth factor changes the pain sensitivity of nerves, helping to reduce pain"*



○ Researchers are developing pain treatments that target nerve growth factor

KILLING PAIN

Damage to our tissues causes mechanical and chemical changes that activate pain-sensing neurons. The neurons send signals to the spinal cord, which relays them to the brain. Painkillers try to block this process by interfering with it at different stages.

The most common over-the-counter painkillers attack the very start of the pain-sensing chain. Non-steroidal anti-inflammatory drugs (NSAIDs) – like ibuprofen – try to remove some of the chemical signals that activate pain-sensing neurons. They do this by interfering with an enzyme called cyclooxygenase (COX). COX makes chemical messengers called prostaglandins, which promote inflammation. Blocking COX dampens the inflammatory response, relieving the pain.

The next step in the pathway is the transmission of pain signals towards the spinal cord. Local anaesthetics work here. For nerve cells to fire they need to transport sodium ions across their membranes. These carry a charge, which sets up the electrical signal. Local anaesthetics block the channels that transport the ions, stopping pain signals in their tracks.

The strongest painkillers, the opioids, work on the next part of the pathway: preventing signals getting to the brain. This group includes codeine, morphine and the illegal drug heroin. They act on the spinal cord and brainstem to stop pain messages passing through.

Finally, there are the general anaesthetics, which work on the very last link in the chain. They stop the brain being aware of pain by interfering with the way that nerve cells pass signals to each other. Each kind of painkiller has advantages and disadvantages for different situations.

○ Painkillers interfere with the way our body senses and responds to damage

OXYCODONE
5/325 TAB
TAKE 1 TABLET BY MOUTH EVERY 3 HOURS AS NEEDED
Qty:30
Refills
Store Phone:
May cause Dizziness

PEOPLE WHO DON'T FEEL PAIN

Very rarely, people are born without the ability to feel pain. A defect in a gene called SCN9A makes it impossible for their pain-sensing nerve cells to transmit signals. This makes it impossible for them to tell when hot becomes burning, when cold becomes freezing or when pressure becomes crushing.

The SCN9A gene codes for a protein that makes a part of a structure called a sodium channel. Sodium ions carry the electrical signals along nerves, and these channels control their movement. With the mutation in the gene, the channels don't fit together and the pain-sensing neurons can't fire. While this might sound like a superpower, but being unable to sense pain makes people with these genetic faults much more likely to do themselves harm.

○ Faults in the SCN9A gene switch pain-sensing nerve cells off by terminating protein translation

GATE CONTROL THEORY

Have you ever stubbed your toe and immediately reached down to grab your foot? Or burnt your finger and instinctively put it into your mouth? This is gate control theory at work.

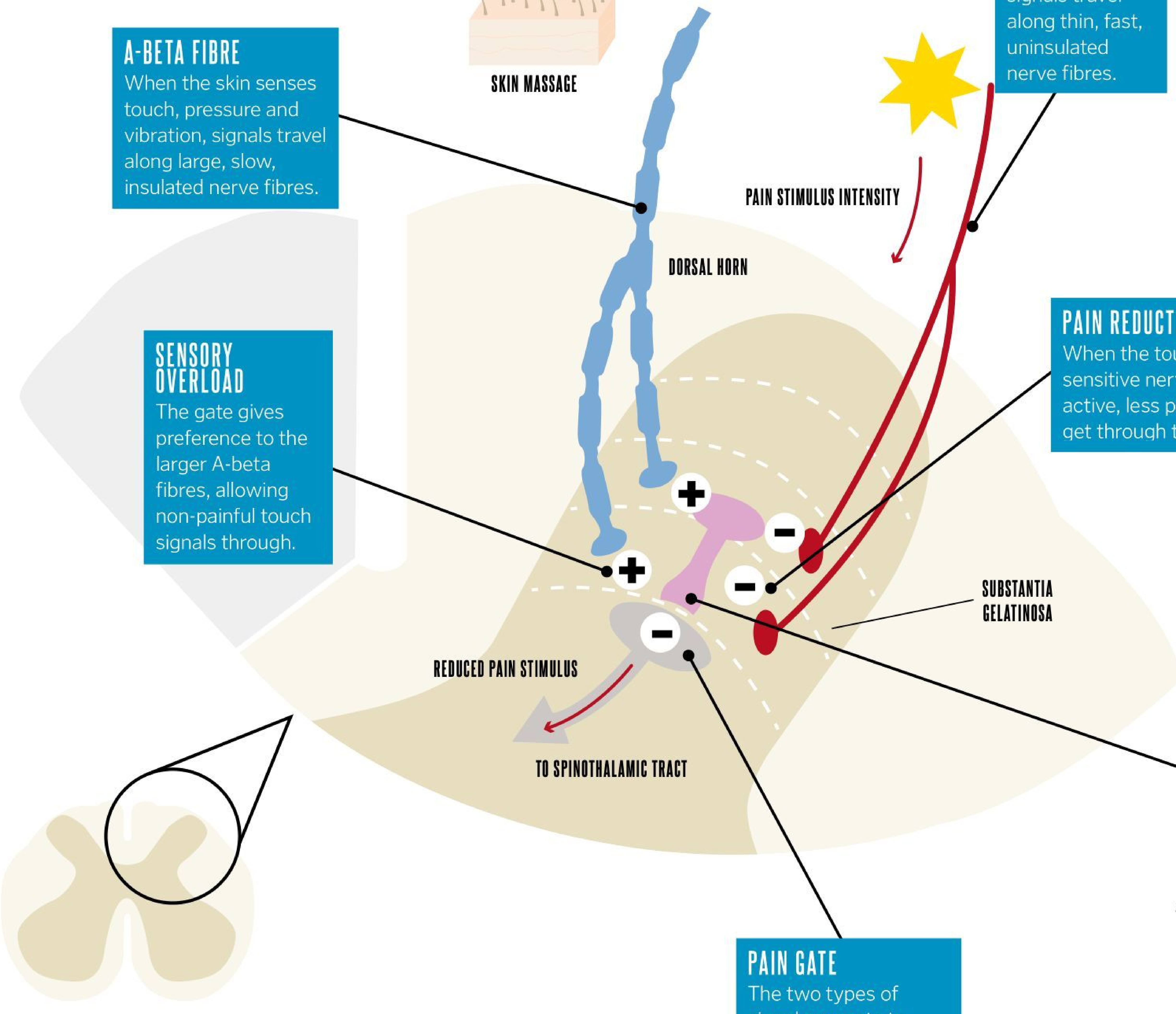
Pain signals travel from the site of an injury towards your brain along thin nerve fibres. As they enter the spinal cord they compete for bandwidth with the other nerves that are also trying to send messages to your brain. This includes larger fibres that carry non-painful signals, like pressure and touch. Both the painful and non-painful signals are trying to reach the projection cells of the spinal cord, but there's a gatekeeper in the way.

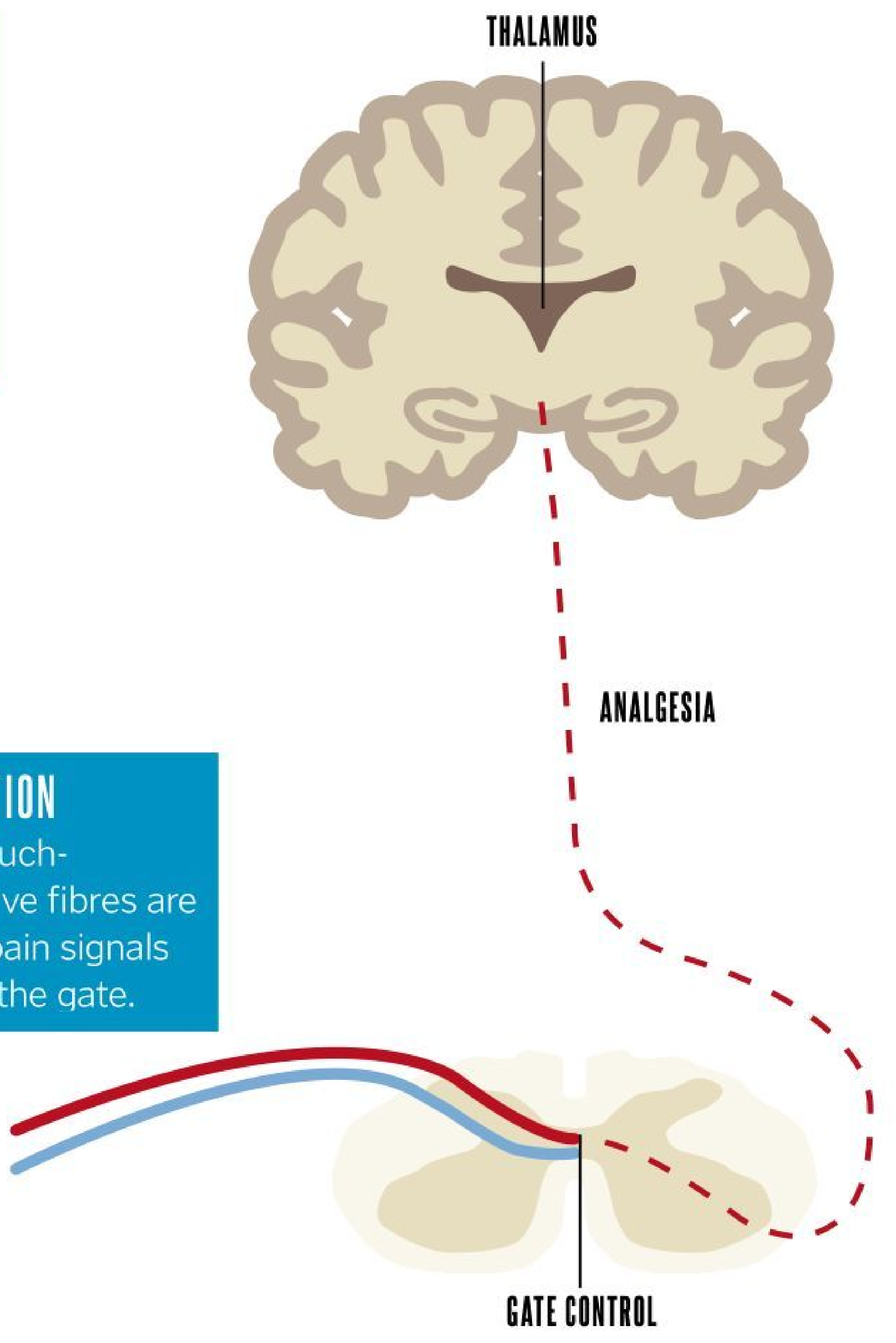
The gatekeeper is an inhibitory neuron. It listens for signals from both the pain fibres and the sensory fibres and decides which can send its signals to the projection neuron. When a pain signal arrives on its own the interneuron lets it through the gate, but when a sensory signal is passing the gate the pain signal closes. So if you put pressure on your stubbed toe it can stop some of the pain signals from reaching your brain, naturally blocking out the unpleasant feeling.

○ Rubbing or holding an injury can override some of the pain signals before they reach your brain

CLOSING THE PAIN GATES

CAN NON-PAINFUL SENSATIONS STOP PAINFUL SIGNALS GETTING TO YOUR BRAIN?





C-FIBRE
When the skin detects damage, signals travel along thin, fast, uninsulated nerve fibres.

A-BETA FIBRE
When the skin senses touch, pressure and vibration, signals travel along large, slow, insulated nerve fibres.

SENSORY OVERLOAD
The gate gives preference to the larger A-beta fibres, allowing non-painful touch signals through.

PAIN REDUCTION
When the touch-sensitive nerve fibres are active, less pain signals get through the gate.

INHIBITORY INTERNEURON
A nerve cell sits between the two fibres, listening for signals and deciding which can pass through.

PAIN GATE
The two types of signal compete to pass through the 'gate' into the spinal cord.

> *"Each kind of painkiller has advantages and disadvantages for different situations"*

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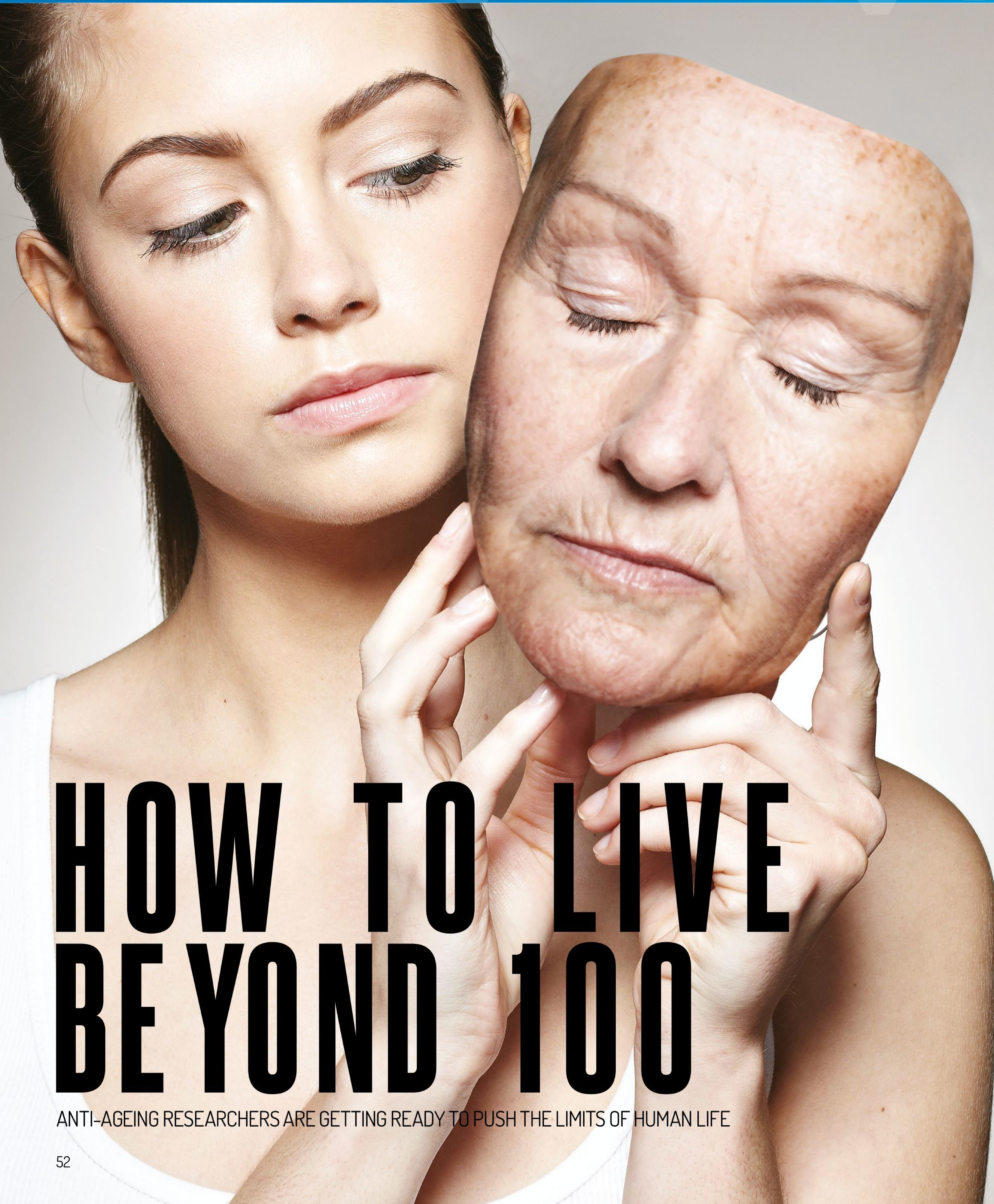


HOW TO LIVE BEYOND 100

ANTI-AGEING RESEARCHERS ARE GETTING READY TO PUSH THE LIMITS OF HUMAN LIFE

We are born, we live, we age and we die. This is the natural cycle of human existence, yet some people live longer than others. The world record holder for the longest human life is Jeanne Louise Calment of France, who lived to a magnificent 122 years and 164 days. But what is the secret to a long life?

Human beings are complex, and we live for a very long time, making studies of the process of ageing a serious challenge. Most of the research to date has therefore been done in animals. Two of the favourite species for these kinds of studies are *Caenorhabditis elegans*, a tiny worm about the size of this comma, and *Mus musculus*, the humble laboratory mouse. The worms generally live for just two or three weeks, while the mice have an upper lifespan of around three years, and both have a lot of genes that are quite similar to our own. Using these models, researchers have identified several possible candidates, including stem cells, calorie restrictio and even some drugs, that could hold off the ageing process.

Scientists across the world have been trying to find the answers for decades, and after years of careful research there is now a wealth of knowledge just waiting to be tested in people. We spoke to Brian Kennedy, CEO of the Buck Institute for Research on Aging. "We're a non-profit medical research institute that's focused on understanding ageing. We realised when the doors opened in 1999 that ageing was the biggest risk factor behind all of the disease that we care about," he explains.

"I think the exciting thing that we have learned over the past decade is that it's really possible to slow ageing in a mouse, or even in primates. The challenge now is to take that knowledge and apply it to humans. We're not just talking about lifespan; what we really want to do is to extend healthspan – the period of time that you're disease-free and functional. The field has amassed a whole load of candidates to slow ageing, and the challenge now is to figure out how to test them."

WHY DO WE AGE?

There is no easy answer to this question. As with almost everything else in biology, it is a combination of genetics and environment. One of the most well-established theories about why we age is that it is an accident of evolution. Charles Darwin's famous theory explains that the 'fittest' or best-adapted animals will reproduce, passing on their genes to the next generation. To get this chance, they need to be able to survive through their early years, find a mate and help their young to make it to adulthood. Over the course of our lifetimes our bodies take damage and start to deteriorate, but after reproduction it doesn't matter so much how long animals live. There is therefore much less pressure to evolve genes that extend life and reverse the damage. In fact, it might even be better in evolutionary terms to live fast and die young, if it means that you have a better chance of passing on your genes.

WHAT MAKES US AGE?

THERE ARE SEVERAL DIFFERENT FACTORS THOUGHT TO CONTRIBUTE TO THE AGEING PROCESS

CALORIES

This is one of the most established areas of research. In mice, rats and even primates, limiting food intake to the minimum requirement can extend lifespan.

DAMAGE

Over time our DNA starts to accumulate mistakes. This is due to damage from the environment as well as errors made when our cells divide.

STEM CELLS

Stem cells can reproduce to replace cells that are damaged or worn out. As we age, they become less able to function, slowing the rate of repair.

INFLAMMATION

Chronic inflammation is found in many age-related diseases, even when there is no infection to fight, but the relationship to aging is unclear.

TELOMERES

The ends of our chromosomes are capped with stretches of protective DNA called telomeres. Every time a cell divides part of this cap is lost.

GLYCATION

Molecules called 'advanced glycation end products', or AGEs, form in our bodies over time. They have been implicated in several age-related diseases.

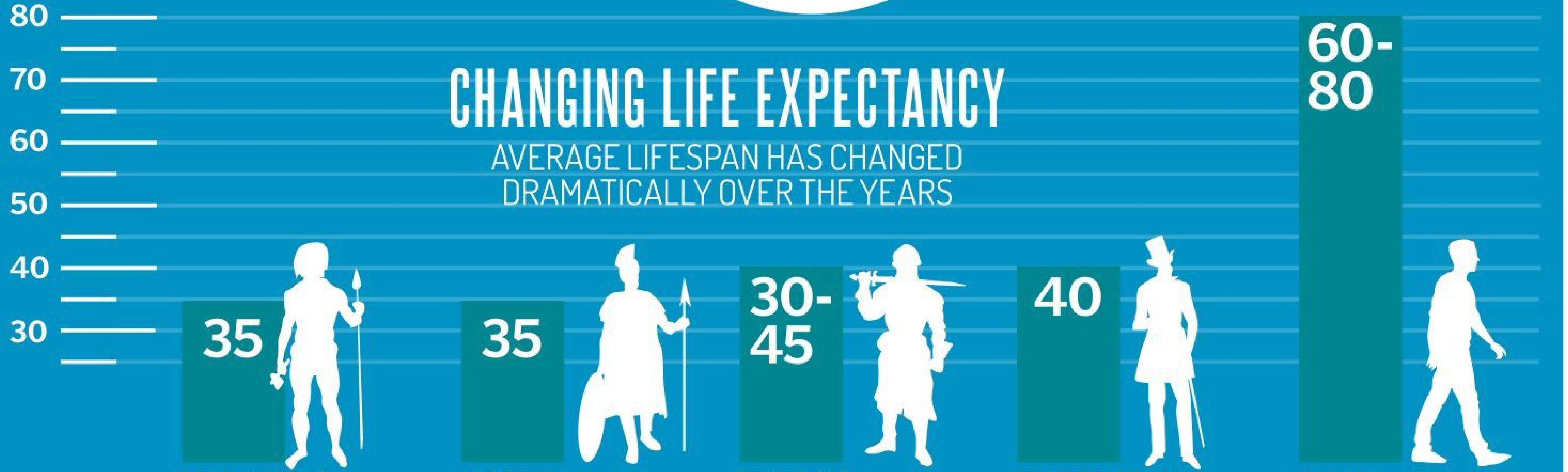
© Getty; Thinkstock; Dreamstime

DO WE HAVE AN AGE LIMIT?

In 2010, an estimated eight per cent of the world's population were over the age of 65. By 2050, this is expected to rise to 16 per cent – that's around 1.5 billion people. But despite this seemingly phenomenal increase in human lifespan, there has actually been little change in the upper limit of human age over the last 2,000 years. Some people were living into their 70s back then, too, as Kennedy explains. "Median life expectancy has been going up at a pretty high rate. But that's median life expectancy. The question of whether we can extend the maximum is still a bit open."

CHANGING LIFE EXPECTANCY

AVERAGE LIFESPAN HAS CHANGED DRAMATICALLY OVER THE YEARS



PREHISTORIC Some prehistoric humans lived into old age, but the majority died young.

CLASSICAL ANTIQUITY Some ancient Greeks and Romans lived into their 70s and beyond.

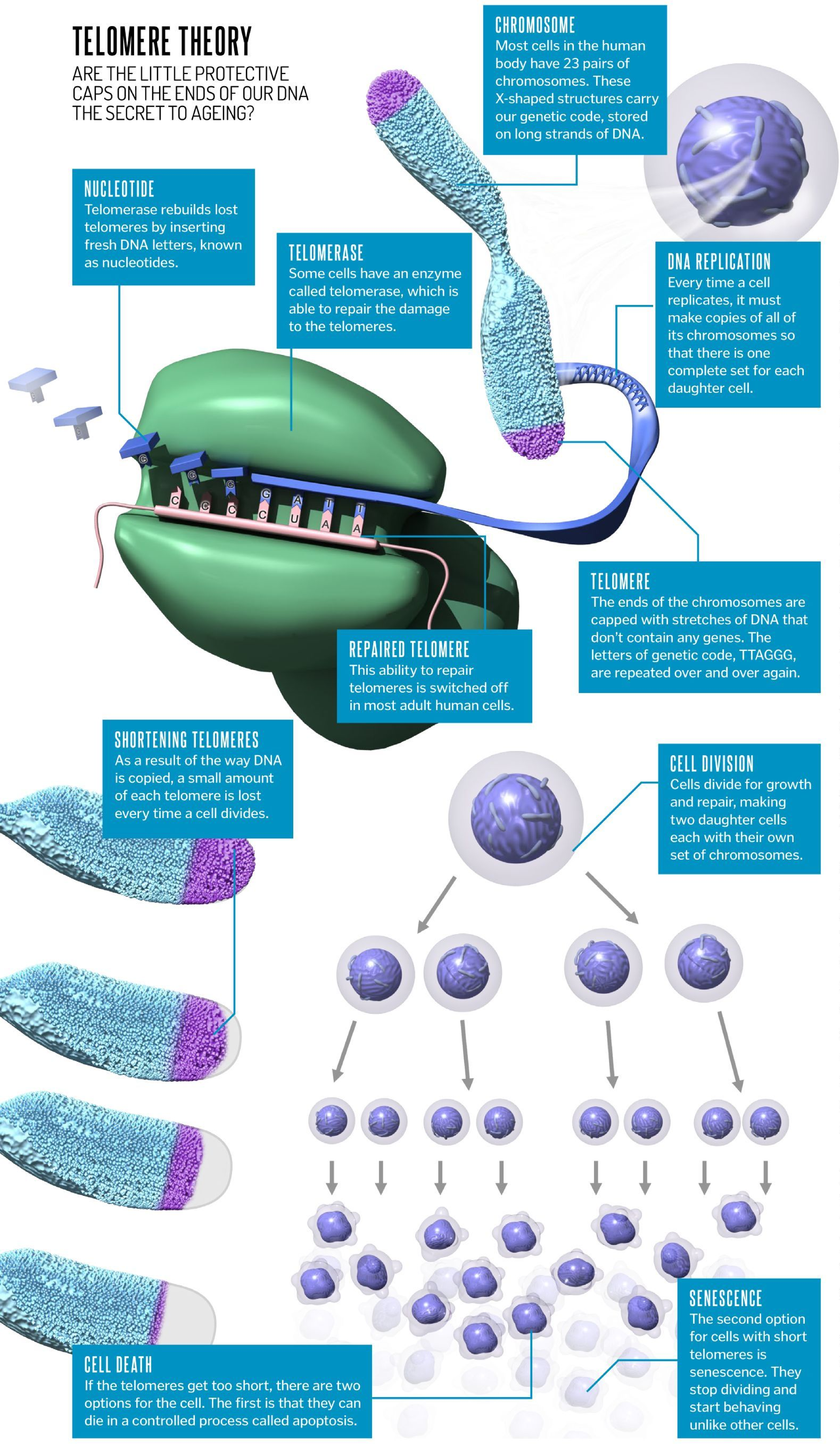
MEDIEVAL Surviving childhood and childbirth were both major challenges.

VICTORIAN At this time, three in ten babies died before they reached their first birthday.

TODAY Life expectancy varies a lot across the world, and it is highest in developed countries.

TELOMERE THEORY

ARE THE LITTLE PROTECTIVE CAPS ON THE ENDS OF OUR DNA THE SECRET TO AGEING?



CHROMOSOME
Most cells in the human body have 23 pairs of chromosomes. These X-shaped structures carry our genetic code, stored on long strands of DNA.

NUCLEOTIDE
Telomerase rebuilds lost telomeres by inserting fresh DNA letters, known as nucleotides.

TELOMERASE
Some cells have an enzyme called telomerase, which is able to repair the damage to the telomeres.

DNA REPLICATION
Every time a cell replicates, it must make copies of all of its chromosomes so that there is one complete set for each daughter cell.

TELOMERE
The ends of the chromosomes are capped with stretches of DNA that don't contain any genes. The letters of genetic code, TTAGGG, are repeated over and over again.

REPAIRED TELOMERE
This ability to repair telomeres is switched off in most adult human cells.

SHORTENING TELOMERES
As a result of the way DNA is copied, a small amount of each telomere is lost every time a cell divides.

CELL DIVISION
Cells divide for growth and repair, making two daughter cells each with their own set of chromosomes.

SENESCENCE
The second option for cells with short telomeres is senescence. They stop dividing and start behaving unlike other cells.

CELL DEATH
If the telomeres get too short, there are two options for the cell. The first is that they can die in a controlled process called apoptosis.

SLOWING THE BODY CLOCK

THE LATEST RESEARCH AIMS TO PUT THE BRAKES ON AGEING AND EXTEND HEALTHY YEARS OF LIFE

Almost all of our cells have 23 pairs of chromosomes. Each chromosome contains a long molecule of DNA wound around a series of proteins to form an X-shape, and the ends are capped with structures known as telomeres. These have been a focus for anti-ageing researchers for many years because every time a cell divides they get a little bit shorter. Eventually, the telomere is so small that the cell can no longer go on dividing.

As Professor Kennedy explains, "If you take cells out of the body and grow them in the test tube, it was found out many years ago that eventually they stop growing. People have thought for 50 years now that this may be a component of ageing." Telomeres can be lengthened again by an enzyme called telomerase, which is found in some stem cells. However, in most adult cells telomerase is switched off. Without it telomeres gradually get shorter as we get older, and our cells start to shut down. Some of these older cells die, while others just stop dividing and become 'senescent', which literally means 'to grow old'.

Researchers at the Buck Institute are very interested in senescence. "One of our investigators, Judy Campisi, has been developing strategies to get rid of senescent cells in the body," he continues. "The problem has always been that there aren't that many senescent cells in the body, even in older people. It might be five per cent of the tissue, ten per cent of the tissue. So the argument was always, 'How can that have that big of an effect if it's only a small proportion of the tissue?' What Judy has found is that these senescent cells secrete factors that have bad effects on the cells in their environment."

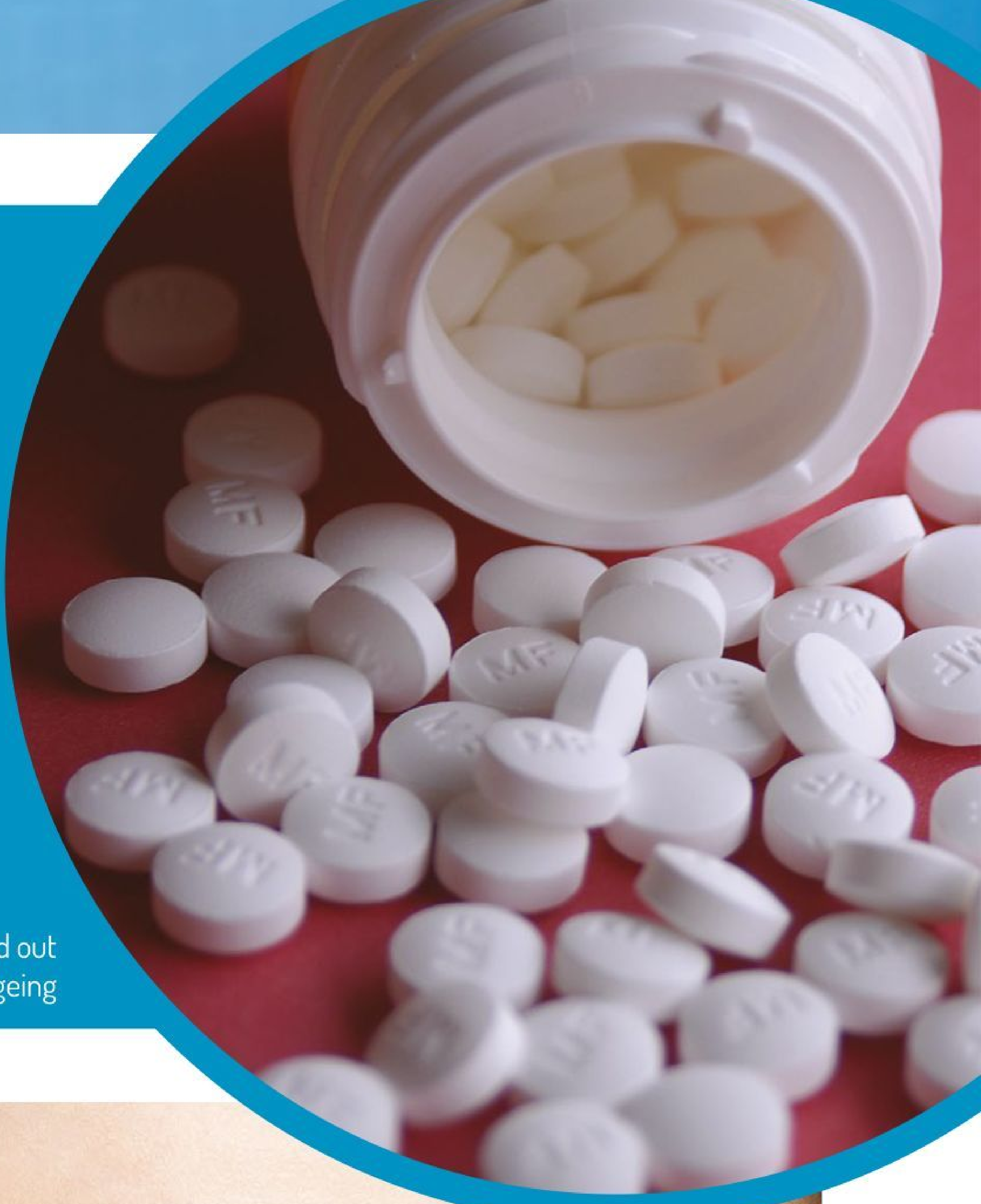
Dr Campisi focused first on investigating the process in mice and has developed a way to kill the senescent cells using genetic engineering. "When you do that, the animals stay healthy longer," Kennedy explains. Dr Campisi is now working on finding a drug that can produce the same results. But the aim isn't necessarily to extend life; these senescent cells could be contributing to age-related diseases, and that's the real focus for the researchers. "Our goal is to keep people healthy and functional longer. They will probably live longer too, but it's really about healthspan more than lifespan".

ANTI-AGEING PILLS

A pill to slow the ageing process might sound inconceivable, but there are actually a few candidate drugs already. Two of the most publicised are rapamycin and metformin. It has been known for a long time that restricting calorie intake can extend the lifespan of mice, and researchers have pinpointed genes involved in a nutrient-sensing pathway called 'target-of-rapamycin' (TOR). When cells have lots of nutrients, this pathway promotes growth, but when nutrients are scarce, it switches the cell over to recycling its own molecules. This switch seems to be critical.

Rapamycin is a drug already used in people to prevent the rejection of transplanted organs, and it dampens the activity of the TOR pathway, helping cells to switch into recycling mode. Rapamycin slows ageing in worms, flies and in mice, but the effects on humans aren't yet known.

An alternative anti-ageing candidate is metformin. This drug decreases the amount of glucose made by the liver and increases uptake of glucose from the blood, and it is already used to treat diabetes. Evidence in worms and some mice shows that metformin can increase longevity, and it also seems to decrease the risk of age-related diseases in people with diabetes. It is not clear whether the drug would have any benefit in healthy people, but researchers in the United States are keen to do a clinical trial to find out.



⬡ Human studies are needed to find out whether these drugs really can slow ageing

THE FUTURE OF ANTI-AGEING

At the moment, most anti-ageing research is focused on extending human healthspan by staving off disease, but we are in the midst of a scientific revolution, and there is no telling what will be available hundreds of years from now. Already scientists can build bionic limbs that respond to the wearer's thoughts, they're learning the incredible potential of stem cells, and they can 3D print structures for transplanting into the body. In the future, some hope that it will be possible to go beyond biology, using these kinds of advances to become 'transhuman' – living longer and ultimately cheating death completely.

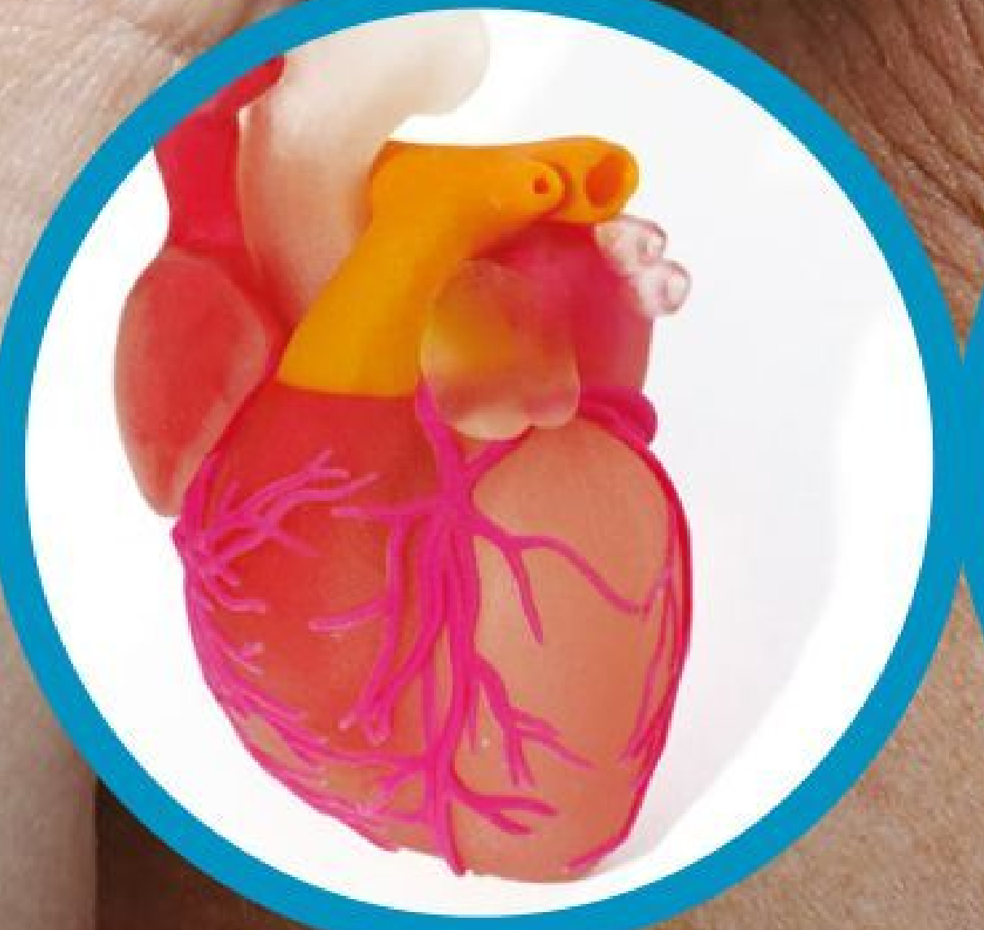
The ideas for transhumanism are limitless and range from augmented body parts through to genetic modification and cloning all the way up to downloading your thoughts onto a memory stick and living forever as a machine. Unfortunately – or fortunately, depending on how you look at it – this future is still a long way off.

> *"Our goal is to keep people healthy and functional longer. It's really about healthspan more than lifespan"* Brian Kennedy

ELIXIR OF YOUTH
Drugs may one day be able to slow the ageing process and help to avoid diseases like Alzheimer's or Parkinson's.

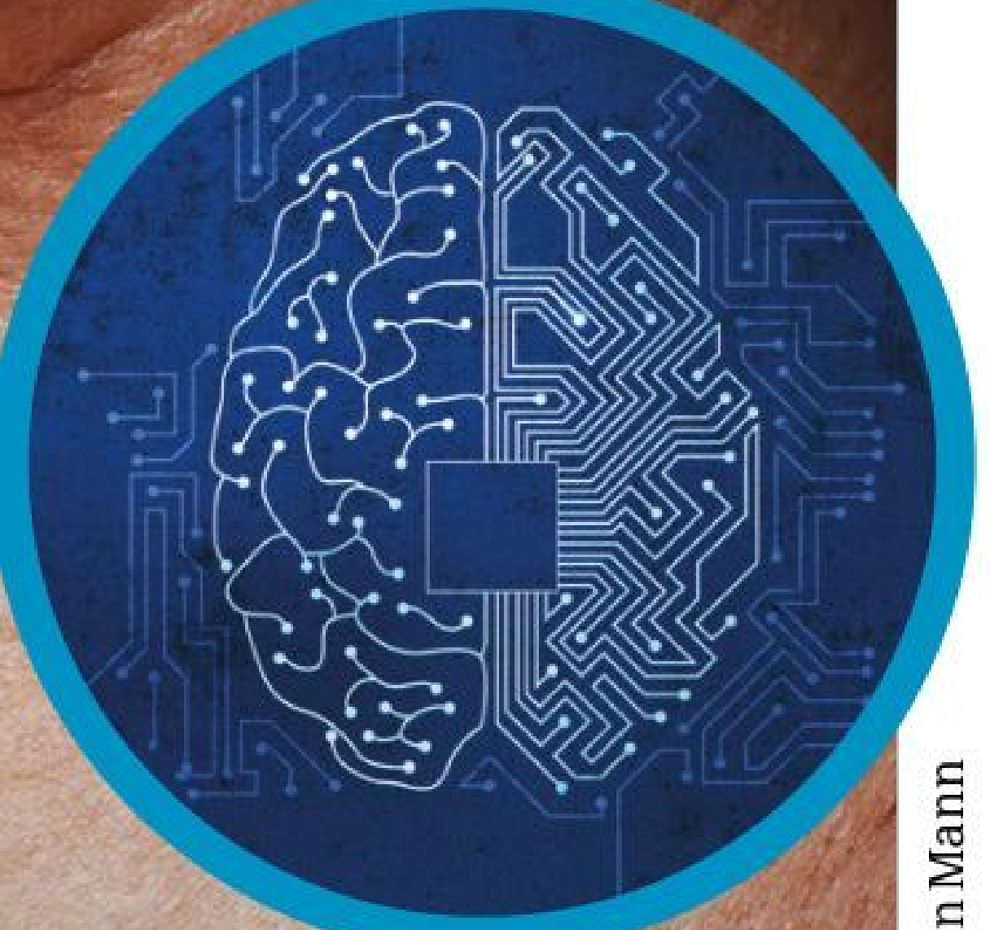
GENETIC ENGINEERING
Editing the youthfulness genes in our genome could change the way that humans age.

CLONING
Fancy living again as an identical version of yourself? Technology could make copies of your cells.



UPGRADING ORGANS
Advanced 3D printing techniques could lead to custom-made organ replacements.

REPLACING LIMBS
Bionic limbs have the potential to be stronger and more durable than the real things.

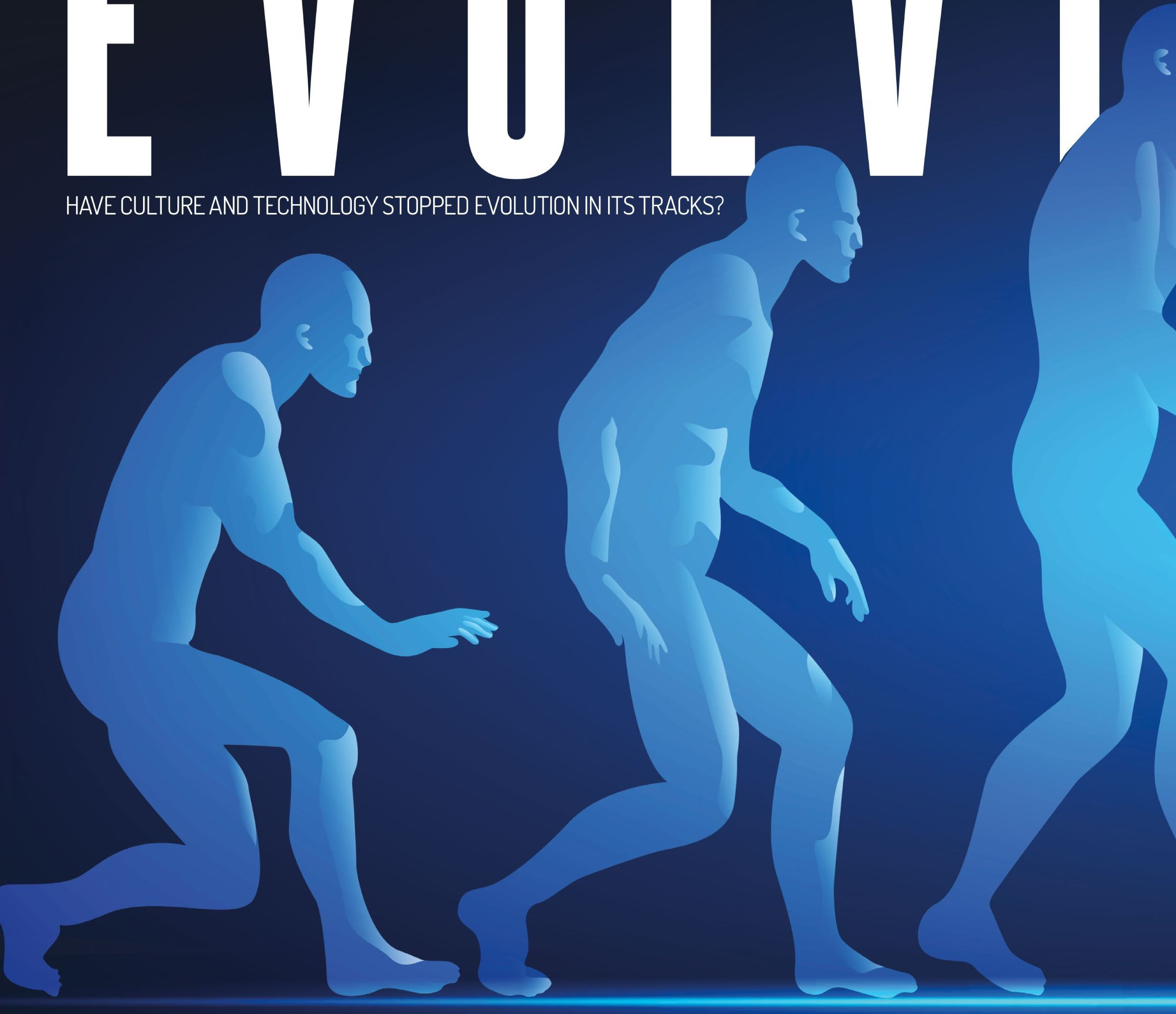


DOWNLOADING YOUR BRAIN
Could we one day replicate the most complex structure in the known universe?

© Getty; Alamy; Illustration by Adrian Mann

ARE WE STILL EVOLVI

HAVE CULTURE AND TECHNOLOGY STOPPED EVOLUTION IN ITS TRACKS?



NG ?

"The genetic differences between us are surprisingly small"

Every human alive today can trace their ancestry back to east Africa around 200,000 years ago – DNA from a single woman still exists in every one of our cells. At the time, the human population was tiny, and her descendants are the only ones still alive today. They spread across the continent 100,000 years ago before radiating out in waves across the world. Scientists know the mother of humanity as mitochondrial Eve.

We may have dispersed, but the genetic differences between us are surprisingly small. There is no major distinction between people living on different continents or people of different races. In fact, there are more genetic differences between subspecies of chimpanzee. This similarity makes people question whether we've stopped evolving completely.

Evolution relies on a few key ingredients. Every generation, an organism makes more individuals than are able to survive. There are differences between those individuals, known as phenotypic variation. The cause of those differences, genes or genotype, are heritable, meaning that they can pass from one generation to the next. Some traits are better suited to the current environment than others. Individuals with those traits are more likely to survive and reproduce, passing the genes for their traits on to the next generation.

New traits enter populations in three main ways, the most well-known of which is mutation. When we make sperm or eggs, cells in our reproductive organs copy their DNA. This process is error-prone, so every time it happens mistakes creep in. This creates tiny changes in the genetic code that pass to the next generation. For the most part the differences don't do anything useful – or harmful. The mutations are often silent (they do nothing) or neutral (they do something, but it doesn't make a difference). In fact, many mutations aren't even in genes;

○ Modern medicine reduces the pressure of illness on our species

© Getty

they're in the DNA that sits between them. However, sometimes mutations change the way a gene works.

New traits can also enter populations via gene flow. This happens when groups of people separate and then come back together, sharing new genetic information. Finally, traits change because of sex. Babies inherit genetic material from both parents, putting new combinations of genes together.

Over the past 100,000 years these three mechanisms have changed the traits that make us human, but we are still young in evolutionary terms. We take a long time to reproduce, and there's a limit to the amount of variation that can accumulate in a few hundred thousand years. Your genetic information only differs from mine by around 0.1 per cent, and most of those differences are single letter changes. Despite outward appearances, the whole human population still shares close family ties.

Our genes are always changing, but genetics is just one piece of the evolutionary puzzle. Our environment has a huge role to play in how our species evolves. For new traits to pass from generation to generation they need to change our chances of survival. This is where Darwin's natural selection comes in. If a genetic change makes an individual more likely to reproduce they have a better chance of passing on their genes. We know this as 'survival of the fittest', but it's not always about being the biggest, strongest or fastest. It's about having traits that let you make the best use of your current environment. As the environment changes, so do the kind of mutations that might be useful.

This is where human evolution gets complicated. We can change our environment with culture, science and technology, messing with natural selection. If you look deep into history, our human-like ancestors were at the mercy of their environment. Lucy, a famous fossil of a species known as *Australopithecus afarensis*, lived 3.2 million years ago. She had ape-like characteristics, including a large jaw, long arms and a covering of fur, but she walked on two legs. She lived in the trees like other apes, but the environment was changing, trees were disappearing, and Lucy was spending more time on the ground. Eggs found near her remains suggest she might have been foraging.

Between Lucy and mitochondrial Eve, climate change eventually forced our ancestors out of the forests and onto the plains. They had to run

○ Agriculture gave us stable access to food, freeing up time for science

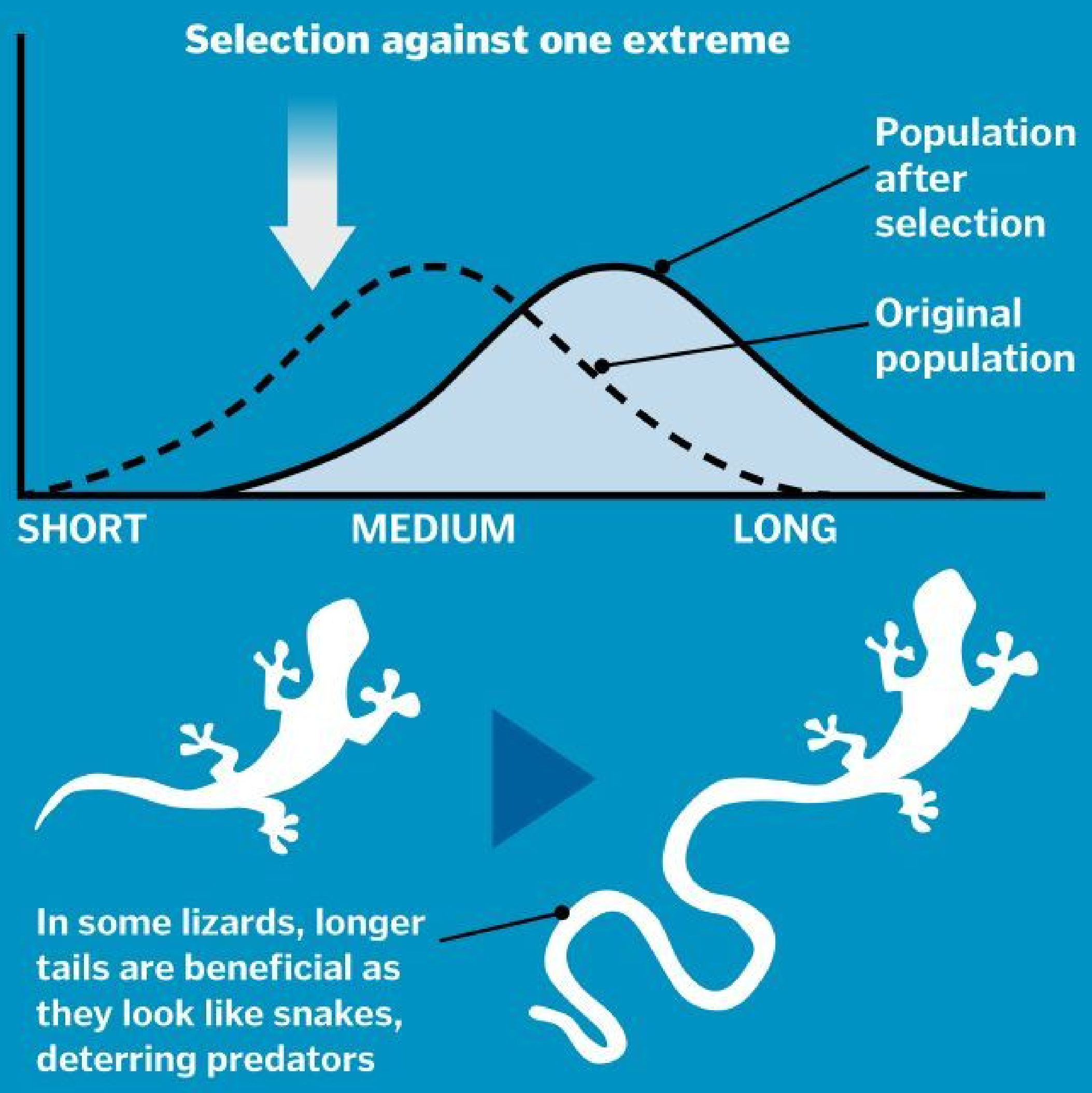
> *"Your genetic information only differs from mine by around 0.1 per cent"*

TYPES OF SELECTION

THREE LAWS OF NATURAL SELECTION GOVERN EVOLUTION, BUT OTHER SELECTIVE FACTORS CAN PLAY A ROLE

DIRECTIONAL

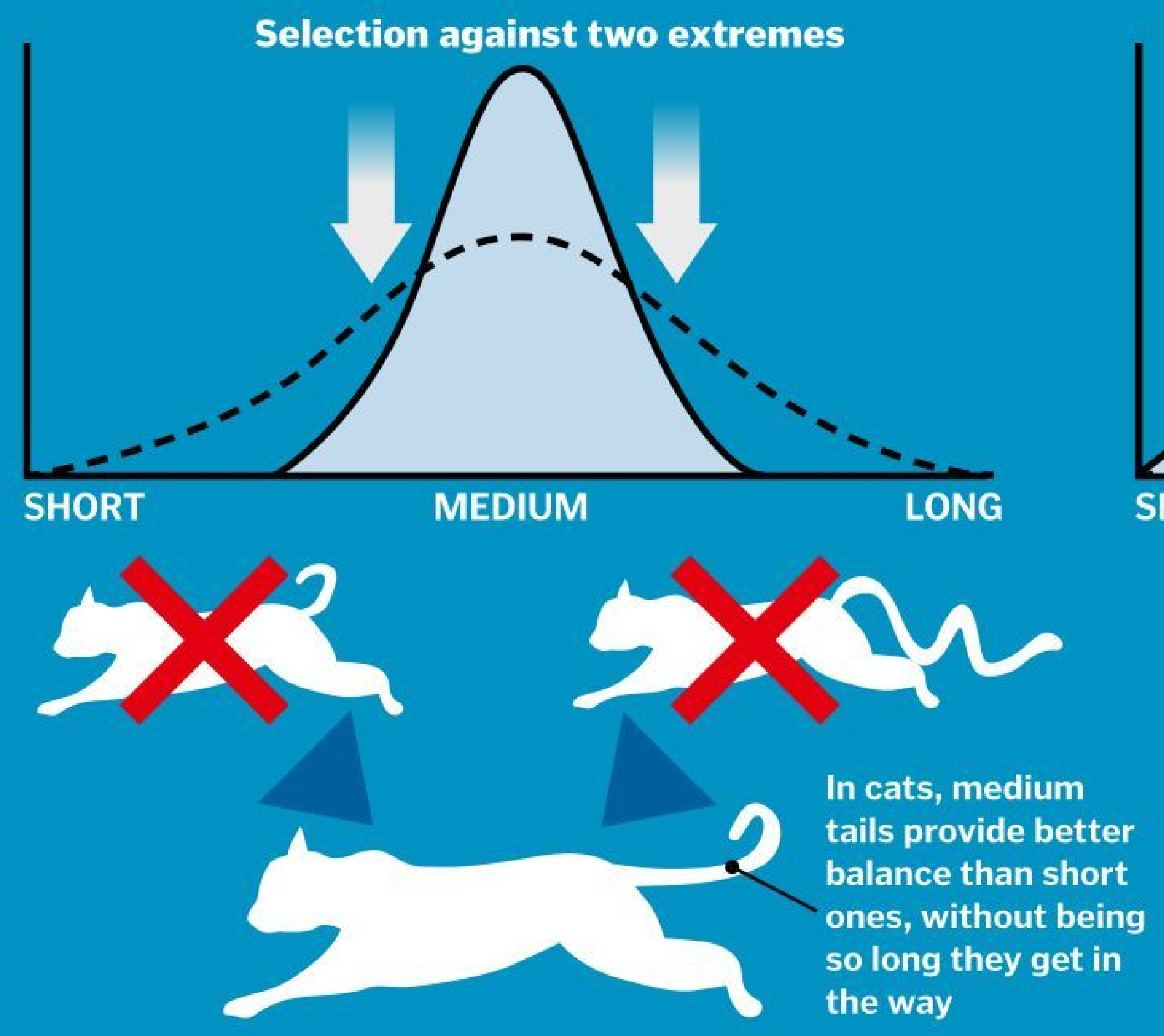
If the environment changes, it forces organisms to adapt. Directional selection pushes traits towards a new solution. Once they find the solution, traits can stabilise again, unless the environment keeps shifting.



In some lizards, longer tails are beneficial as they look like snakes, deterring predators

STABILISING

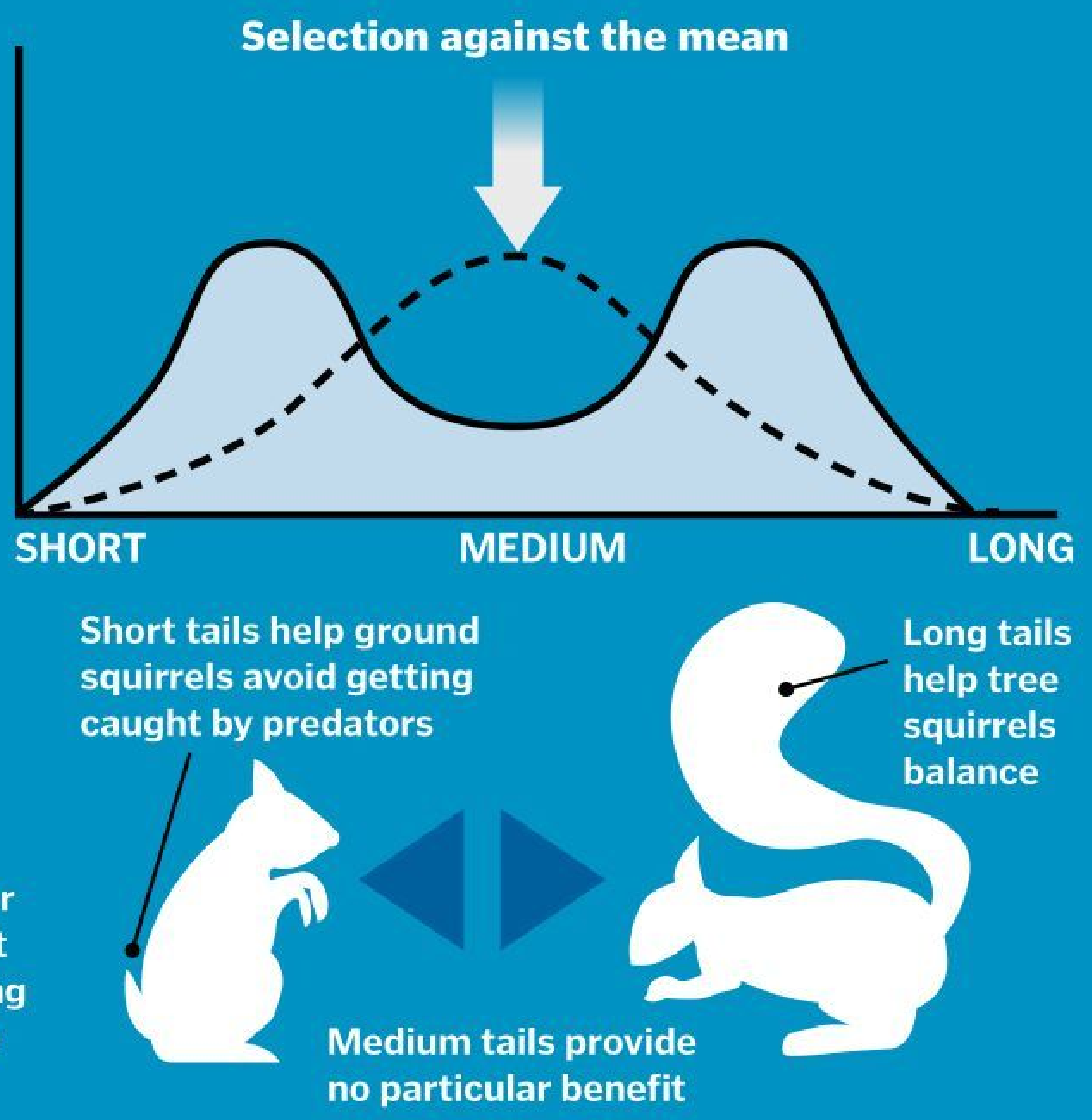
This encourages organisms to keep the same traits. This tends to happen when the environment is stable and the organism is already adapted. Any changes make them less likely to pass on their genes.



In cats, medium tails provide better balance than short ones, without being so long they get in the way

DISRUPTIVE

Sometimes there is more than one way to adapt to environmental change. In these situations organisms evolve away from the middle ground and towards one of two extremes. If this persists a population may split.



Short tails help ground squirrels avoid getting caught by predators

Long tails help tree squirrels balance

Medium tails provide no particular benefit

SEXUAL

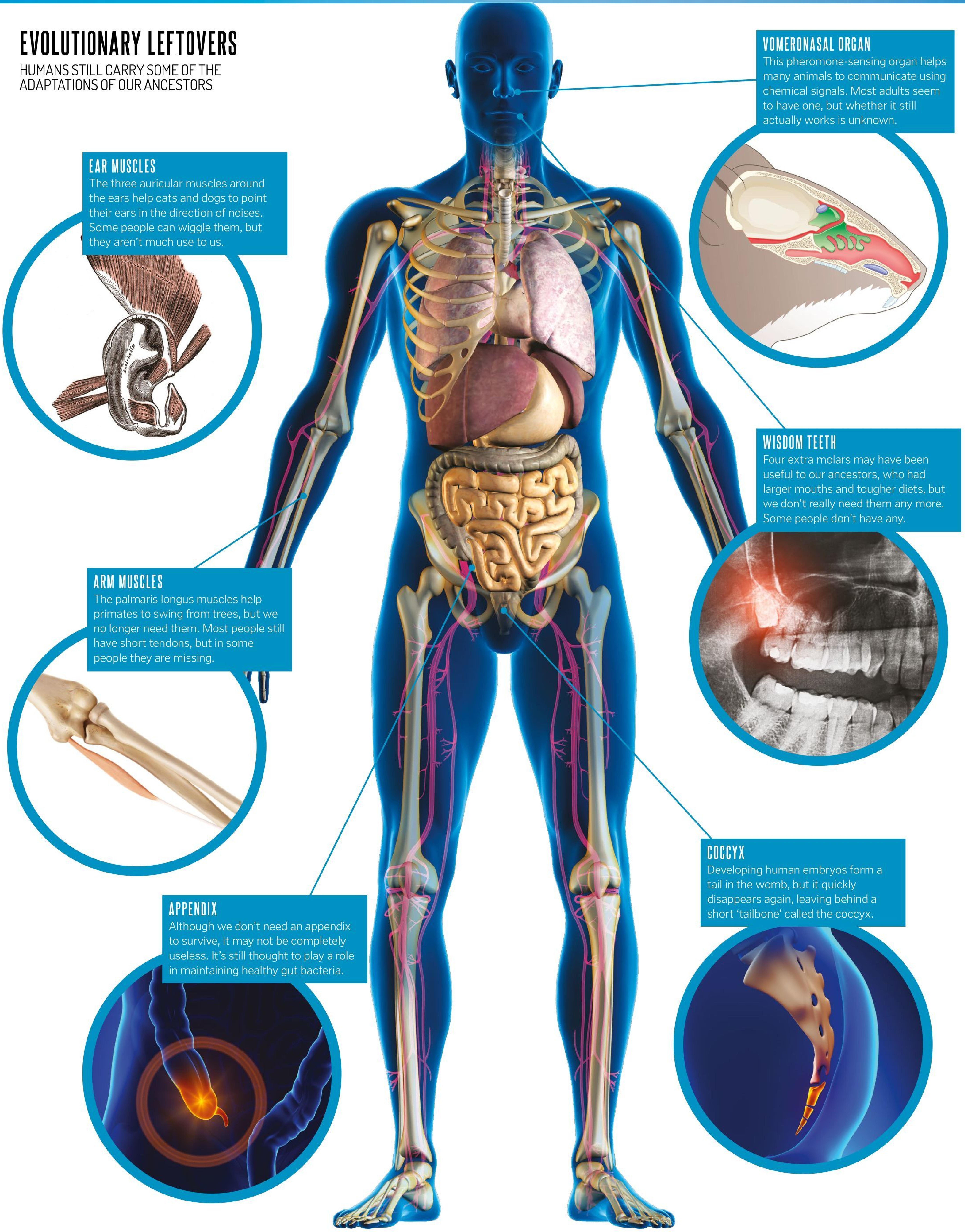
Natural selection favours animals best suited to their environment, but it's not the only way. Sexual selection favours traits that make individuals more attractive and more likely to reproduce, even if they don't help them to survive.

ARTIFICIAL

Artificial selection works in the same way as natural selection, except that we make the decisions. By choosing which animals to breed, we dictate which traits are passed on.

EVOLUTIONARY LEFTOVERS

HUMANS STILL CARRY SOME OF THE ADAPTATIONS OF OUR ANCESTORS



EAR MUSCLES
The three auricular muscles around the ears help cats and dogs to point their ears in the direction of noises. Some people can wiggle them, but they aren't much use to us.

ARM MUSCLES
The palmaris longus muscles help primates to swing from trees, but we no longer need them. Most people still have short tendons, but in some people they are missing.

APPENDIX
Although we don't need an appendix to survive, it may not be completely useless. It's still thought to play a role in maintaining healthy gut bacteria.

VOMERONASAL ORGAN
This pheromone-sensing organ helps many animals to communicate using chemical signals. Most adults seem to have one, but whether it still actually works is unknown.

WISDOM TEETH
Four extra molars may have been useful to our ancestors, who had larger mouths and tougher diets, but we don't really need them any more. Some people don't have any.

COCCYX
Developing human embryos form a tail in the womb, but it quickly disappears again, leaving behind a short 'tailbone' called the coccyx.

under blazing sunshine to survive, and body hair became a burden. Bare skin and the ability to lose heat by sweating became an advantage. Pressure from the environment pushed the genes of our ancestors to change.

Over time, early humans evolved bigger brains, smaller jaws and complex social structures. We harnessed fire and invented tools, and as we became more intelligent we made more and more changes to our environment. This changed everything.

The advent of agriculture around 10,000 years ago caused a seismic shift in human history. Suddenly, we could produce our own food on demand, right next to our homes. DNA from ancient humans has revealed that changing our own environment changed at least 12 regions of our genetic code.

Researchers at Harvard Medical School examined the remains of 230 people who lived between 8,500 and 2,300 years ago. They found differences in genes involved in height, metabolism and skin pigmentation. Around 4,000 years ago, a mutation appeared that allowed adults to keep digesting milk. Light skin became more common, which the researchers believe may have been a response to less vitamin D in a plant-based farmer's diet. The immune system also changed, which may have helped people to live closer together.

We share behaviours that we learn during our lifetimes, passing information from generation to generation like genes. Learning and culture change our environment, changing the pressures that drive selection. This kind of genetic and cultural co-evolution isn't unique to humans. Whales and dolphins are some of the most intelligent animals on the planet, and there is evidence that they also evolve in response to learning.

Killer whales can tackle many different types of prey, but certain groups prefer different meals. In the North Atlantic, for example, some like salmon, some prefer mammals, and others eat sharks. These cultural preferences pass from mother to baby, and because the groups don't tend to mix, they stay the same across generations. Scientists found differences in the genetics of whales that eat fish versus those that eat mammals. We changed our genes by learning to farm, and they've changed theirs by choosing which prey to eat.

This cultural learning helps us to keep adapting, but humans have taken it further than any other animal. We made clothes and complex shelters. We domesticated plants and animals to provide a steady source of food. We built boats, cars and planes to explore the world. We invented medicine to treat injuries and disease. We made it possible to choose when – and if – to have children. We can even survive in space. We have secured our environment, reducing the pressures that push other species to change over time. Reducing those pressures freed up even more time for new ideas and new technologies. Science has made it possible to change our environment more than ever before, but does that mean that we've stopped evolving?

It's hard to see evolution in action in human populations today because we have such a long lifespan, and even when natural selection isn't happening, our genes continue to mutate, a phenomenon known as genetic drift. However, there is one serious selective pressure that we still don't have under control: disease. If you look into its past you can see how modern humans have changed in recent years.

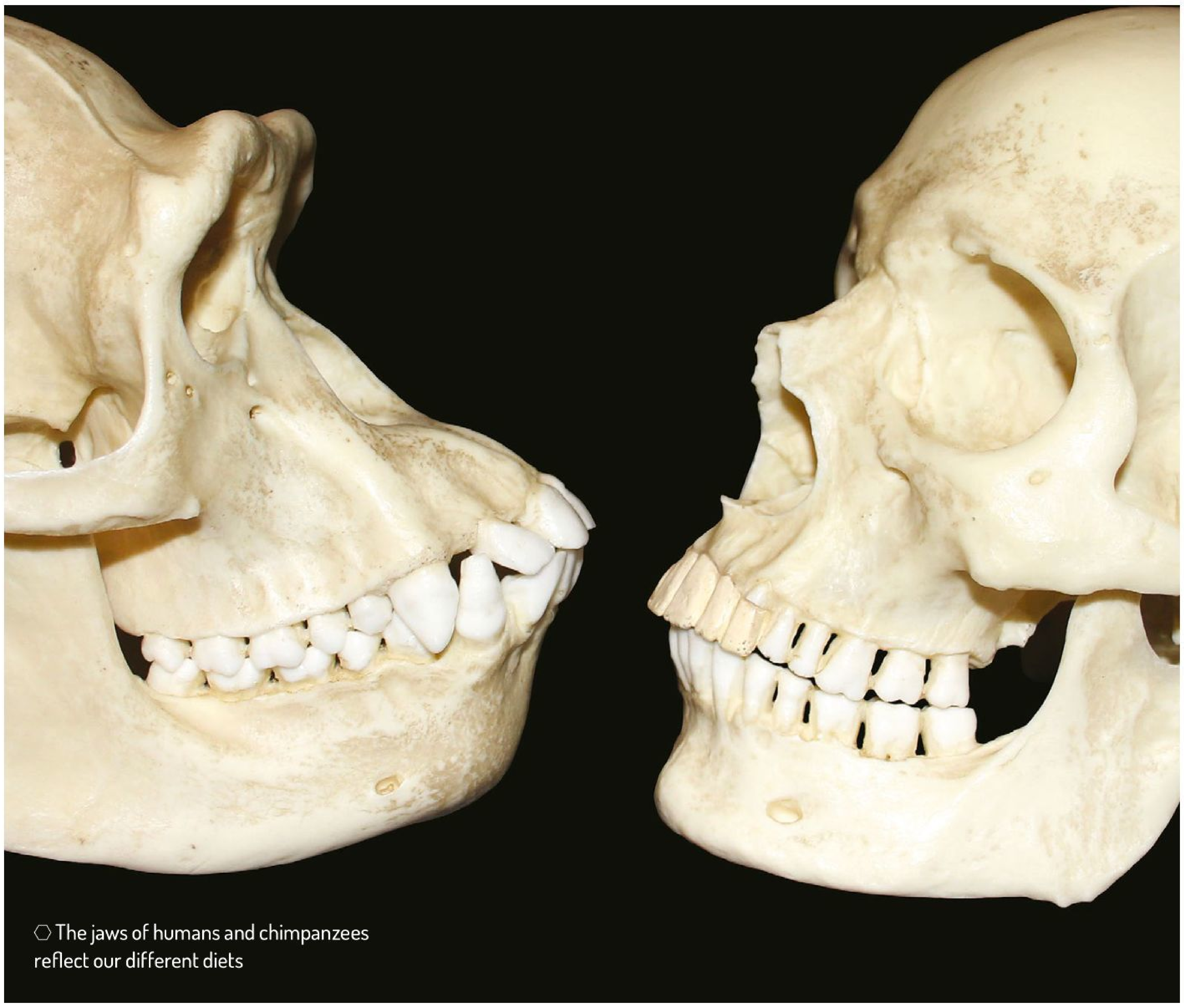
The plague ripped through Europe around 750 years ago, killing vast numbers of people. When our species faces diseases we can't yet treat,

ONGOING EVOLUTION

Two recent studies have found evidence to suggest that we are indeed still evolving, albeit very slowly. Among smokers, those with a variant of a gene known as CHRNA3 are associated with smoking more heavily than average. Being a heavy smoker increases the risk of dying from a smoking-related disease, such as lung cancer. Scientists found that, between generations of 80-year-olds and 60-year-olds, the variant of this gene has decreased by about one per cent. However, until further data is collected from younger generations, this trend cannot be confirmed.

A similar decline seems to be emerging in those with a variant of the gene ApoE4, which increases the risk of developing late-onset Alzheimer's and cardiovascular disease. One possible explanation for both these gene variants becoming rarer is that more people are having children later. The number of people waiting until their 40s or 50s to start a family is increasing, but this is also the age at which people with such gene variants may be at risk of dying.

⬡ Smokers with a variation in the CHRNA3 gene are more likely to be heavy smokers



⬡ The jaws of humans and chimpanzees reflect our different diets

⬡ The development of technology will continue to shape the future of our species

⬡ Changes to our genes are only part of our evolutionary story

> "Cultural learning helps us to keep adapting"

natural selection takes over. Scientists think that's why modern populations in Northern Europe have a higher frequency of a mutation in a gene called CCR5. This gene codes for a molecule used by the immune system, and it provides protection against the plague bacteria, *Yersinia pestis*. It also protects against the HIV virus. People with the protective trait were more likely to survive, and their descendants are still alive today.

As a species we have outsourced huge parts of our survival to technology. We control our environment to maintain a steady state, reducing the pressure that forces genes to change, but to keep this going we need our environment to stay the same, and we haven't worked it all out yet.

What happens when the climate changes, or when antibiotics no longer work as they should? We have buffered ourselves against natural selection for the moment, but we haven't out-evolved evolution.

FUTURE HUMANS

Work is underway to extend our understanding of evolution beyond the ideas set out by Darwin. It's not just genetic inheritance that affects our evolution; the environment that our parents pass on changes us too. In new environments different genes become more or less useful to our survival. By changing our environment we change the selective pressures that drive our species forward. In biology this process is known as niche construction.

Data suggests that cultural evolution has already changed the way that our genes evolved by affecting the type of selection we are under. Even so, our genes don't always need to change for our species to adapt. We can change our environment much more rapidly than we change our genes, allowing us to thrive in situations that our biology couldn't handle alone. Computer simulations suggest that this kind of cultural evolution could work in a similar way to genetic evolution, only faster. Who knows where that will take us as human culture continues to change and technology continues to improve.

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SCIENTIFIC PROGRESS

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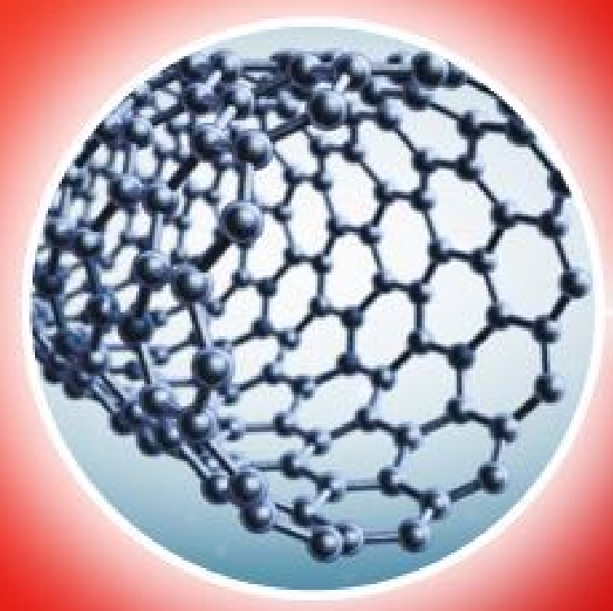

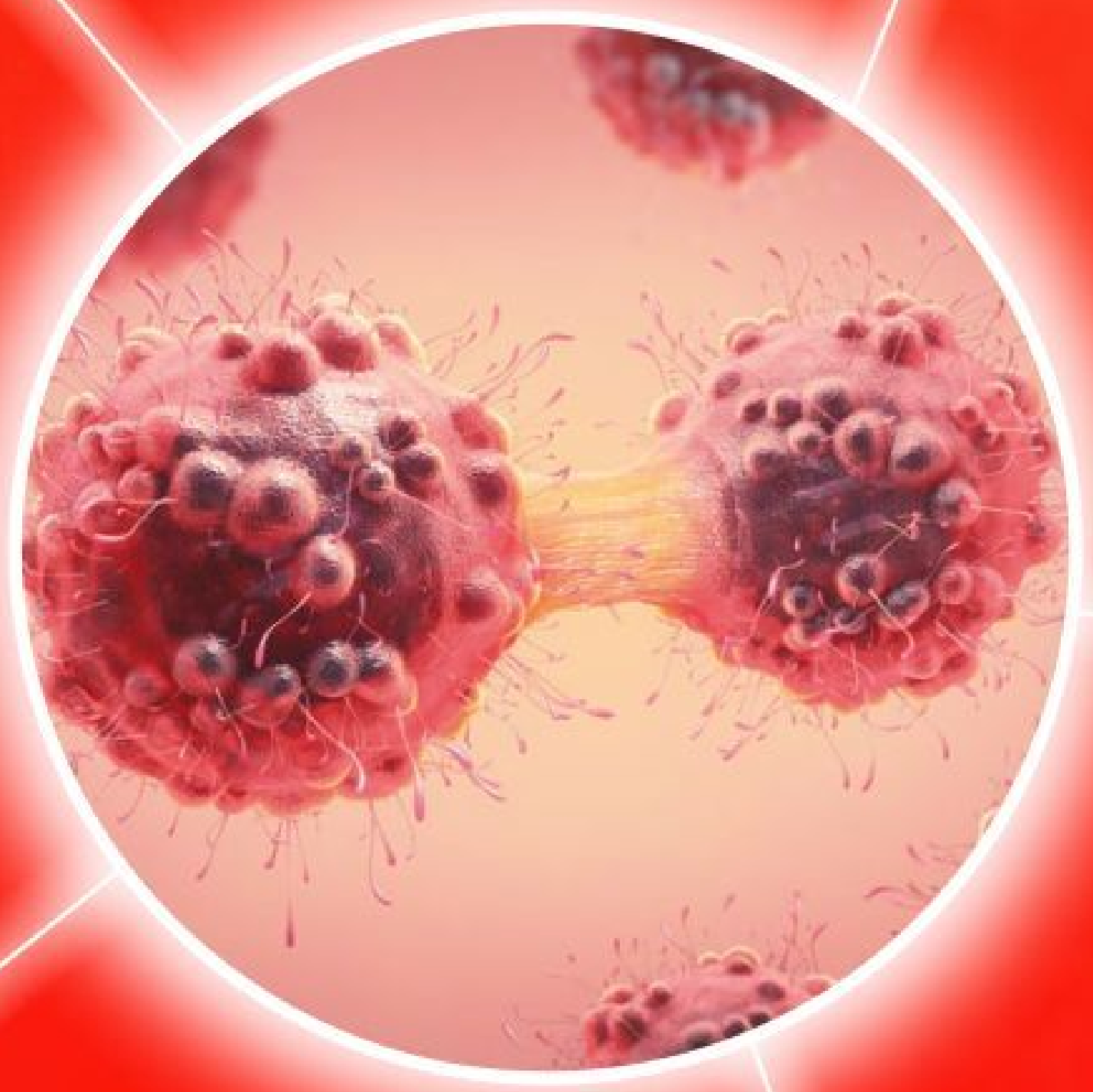

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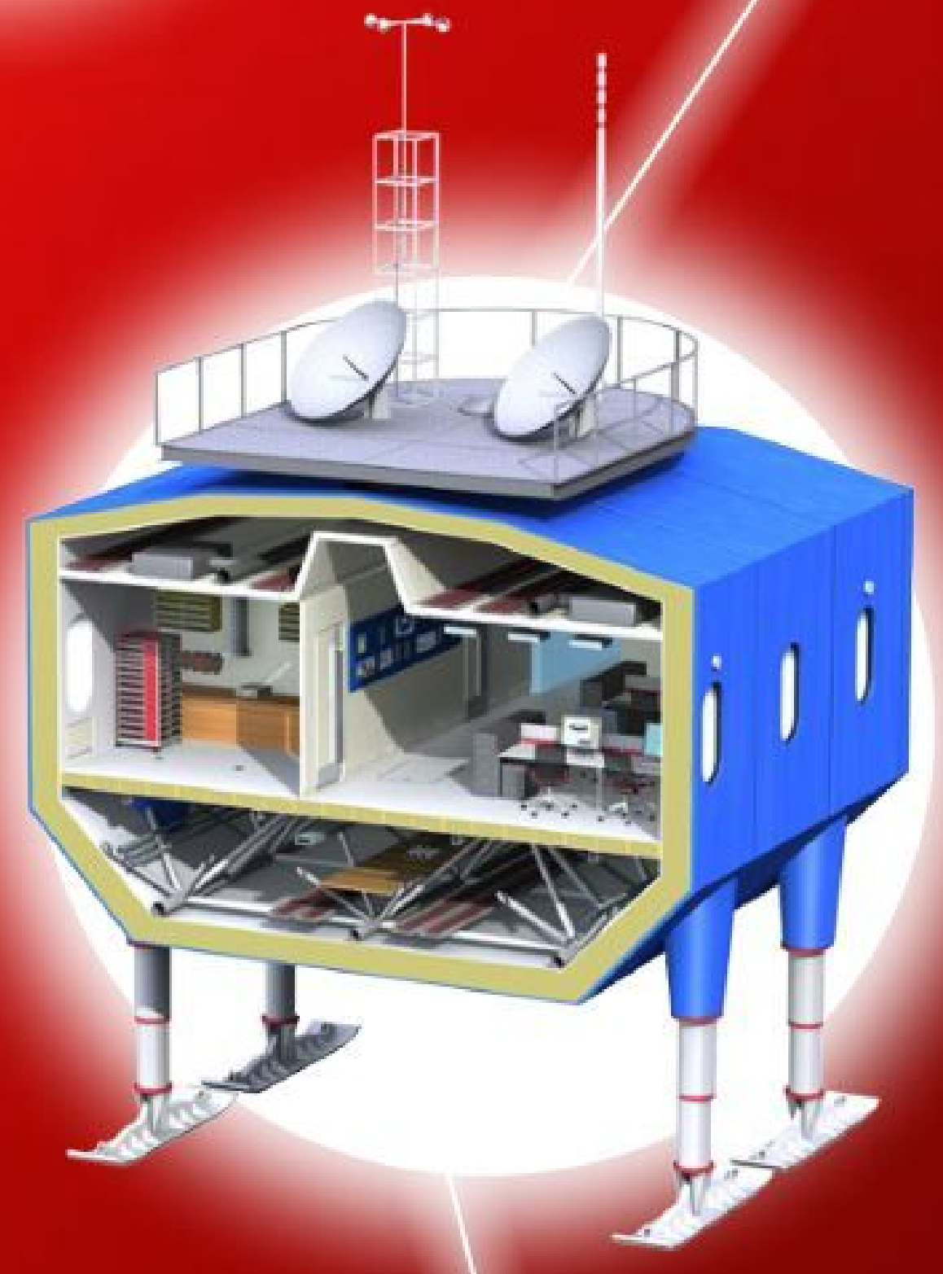

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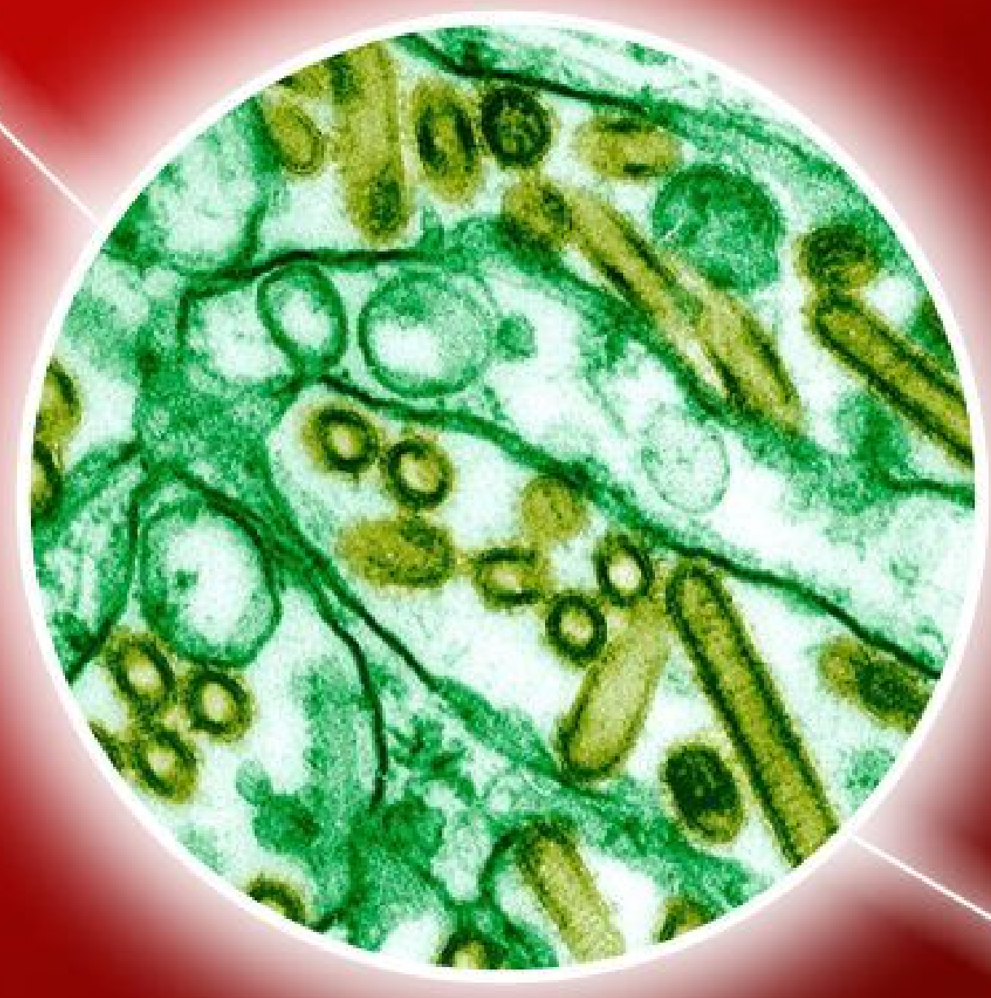

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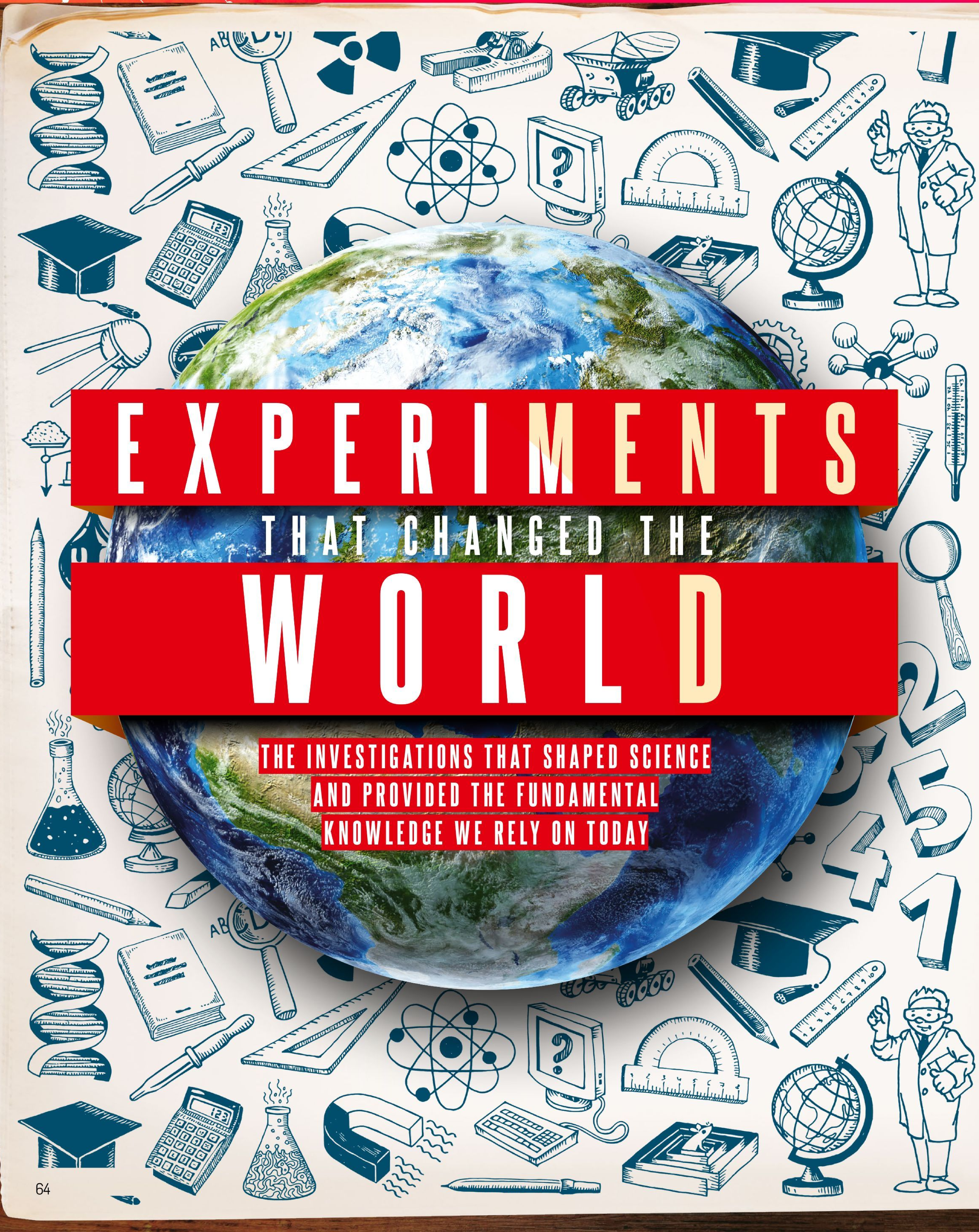


EXPERIMENTS THAT CHANGED THE WORLD

THE INVESTIGATIONS THAT SHAPED SCIENCE AND PROVIDED THE FUNDAMENTAL KNOWLEDGE WE RELY ON TODAY

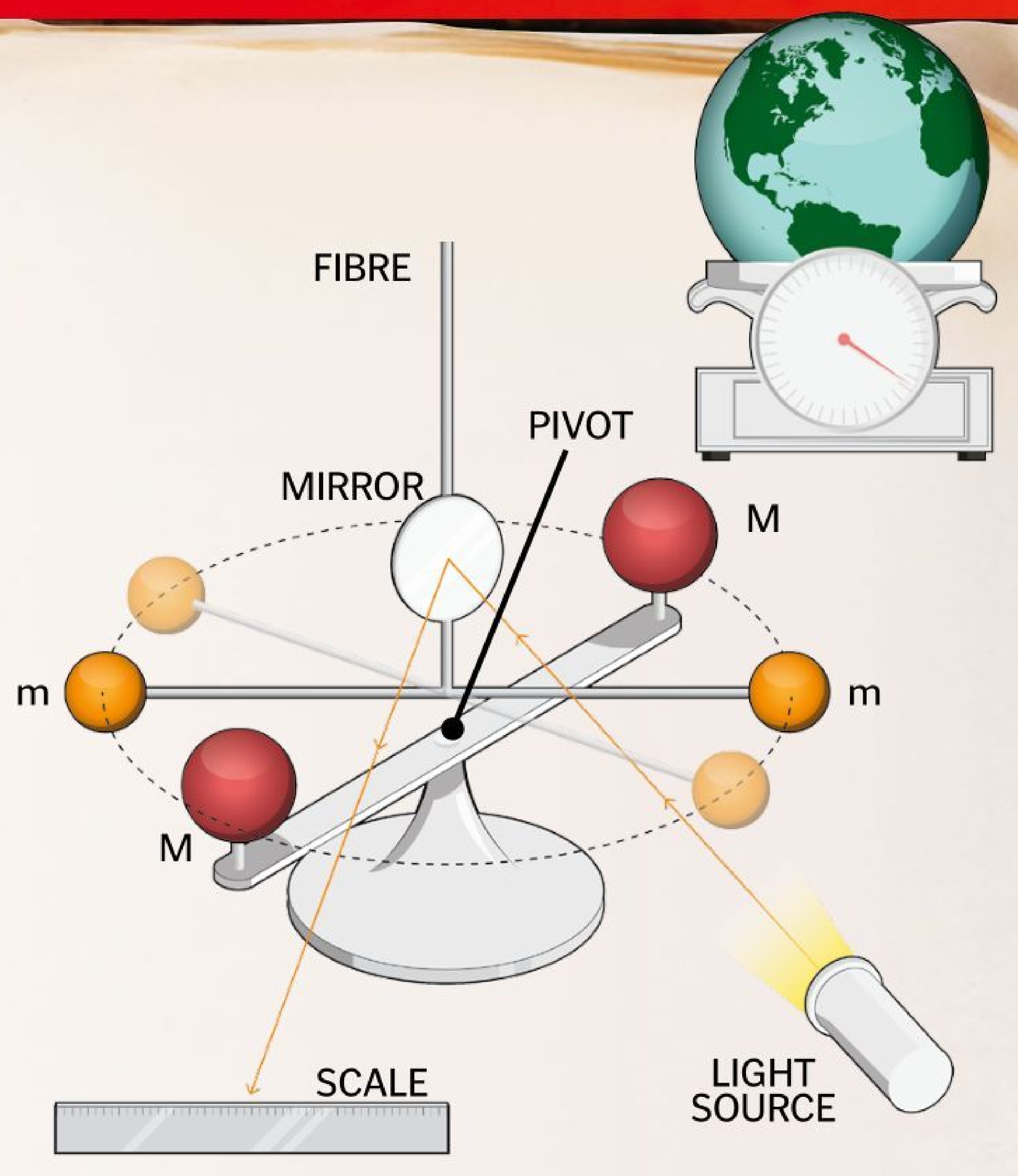
CAVENDISH WEIGHS THE WORLD

ENGLAND, 18TH CENTURY

Not only did the solitary and eccentric Henry Cavendish discover hydrogen, but he also successfully measured the weight of the world. His ambitious experiment used a special piece of equipment called a torsion balance, and in 1798 he reported his results. By measuring the gravitational attraction between two different sized lead spheres he managed to calculate the Earth's density.

The apparatus consisted of a 1.8-metre wooden rod that had a 0.73-kilogram lead sphere attached to each end suspended from a wire. A separate system of two larger 159-kilogram lead balls was placed close to the smaller balls. This exerted enough gravitational force so that when the weights were tugged slightly the rod twisted (a telescope was used to observe this). Cavendish performed his experiments in a dark and wind-proof room to prevent any external air currents and temperature differences affecting his results. He was able to calculate the Earth's density by using the ratios of the forces between the spheres and the gravitational attraction of the Earth to the spheres.

Incredibly, his results were very accurate, and his great experiment meant we could also calculate the mass of the Sun and the Moon and even other planets in our Solar System.



Cavendish's experiment to measure the weight of the world yielded results almost as accurate at today's calculations

GALILEO GALILEI AND THE LEANING TOWER OF PISA EXPERIMENT

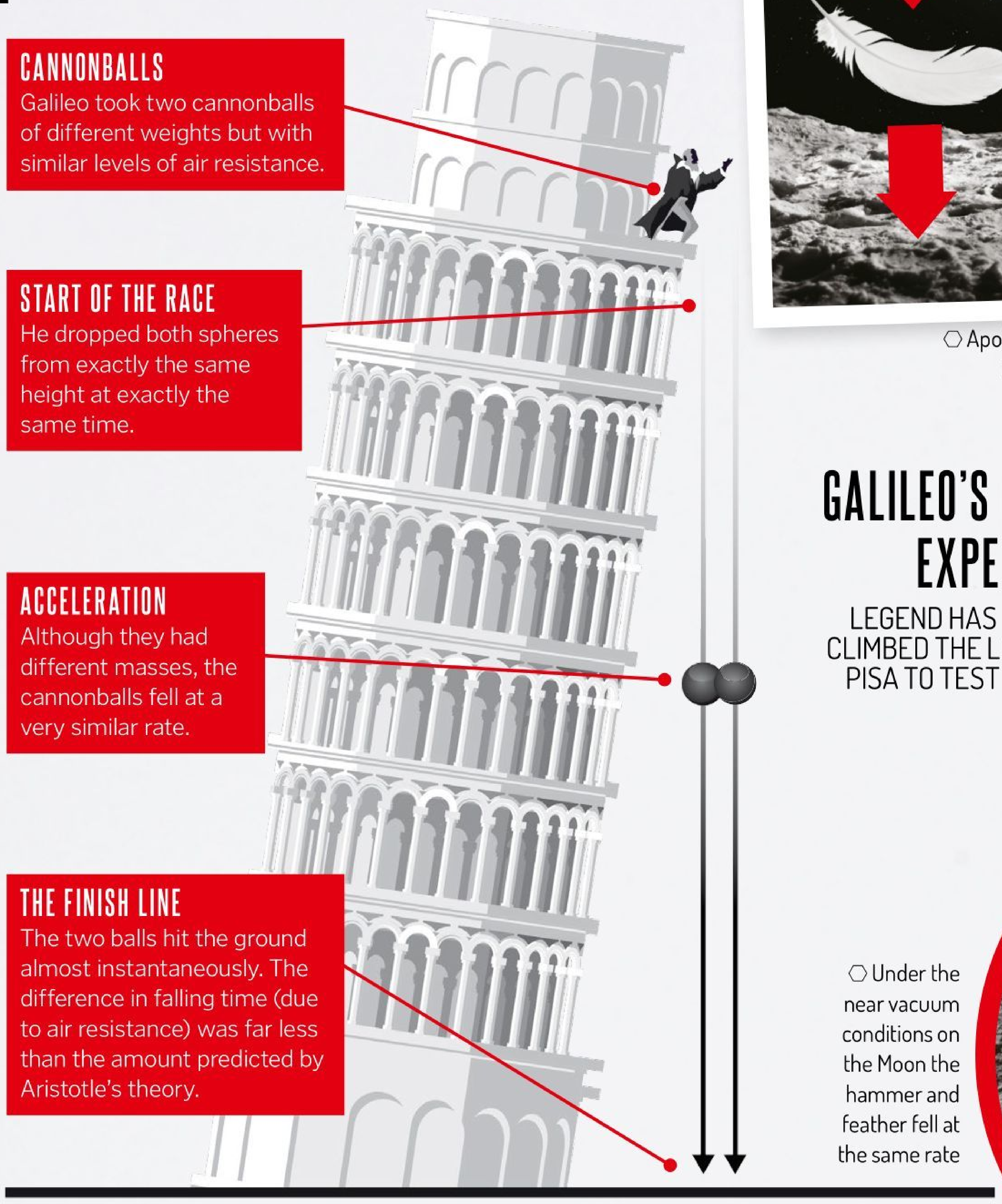
ITALY, 16TH CENTURY

Imagine you drop a bowling ball from one hand and a feather from the other. Which will fall faster? It is obviously the bowling ball, but this doesn't reflect the nature of the force of gravity.

Greek philosopher Aristotle had proposed that objects fell at different rates because gravity would act more strongly on heavier objects, but it turns out that the feather falls slower only because of air resistance. If you could perform the same experiment in a vacuum the feather and ball would hit the ground at exactly the same time.

It is difficult to separate fact from legend, but the story goes that Aristotle's theory of gravity went unchallenged until Italian polymath Galileo Galilei disproved it. Though he spent the last years of his life imprisoned for going against the popular beliefs of the time, his work on speed, velocity, gravity and free fall provided the foundations of the understanding of how the planets and Solar System moved.

Hundreds of years after his death his experiment was repeated on the Moon – unsurprisingly, Galileo was right.

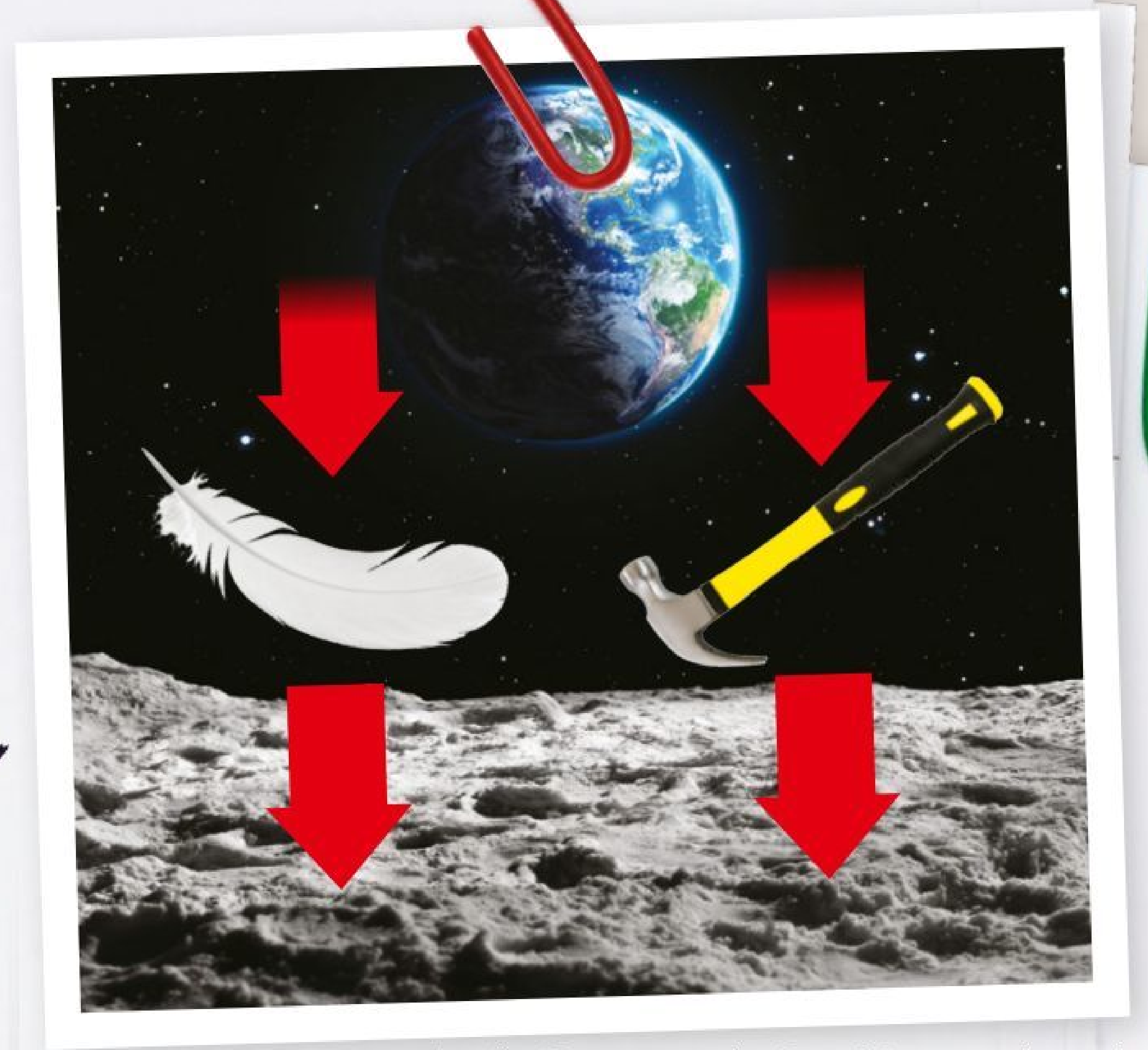


CANNONBALLS
Galileo took two cannonballs of different weights but with similar levels of air resistance.

START OF THE RACE
He dropped both spheres from exactly the same height at exactly the same time.

ACCELERATION
Although they had different masses, the cannonballs fell at a very similar rate.

THE FINISH LINE
The two balls hit the ground almost instantaneously. The difference in falling time (due to air resistance) was far less than the amount predicted by Aristotle's theory.



Apollo 15 commander David Scott replicated Galileo's experiment on the Moon in 1971

GALILEO'S CANNONBALL EXPERIMENT

LEGEND HAS IT THAT GALILEO CLIMBED THE LEANING TOWER OF PISA TO TEST HIS HYPOTHESIS

Under the near vacuum conditions on the Moon the hammer and feather fell at the same rate

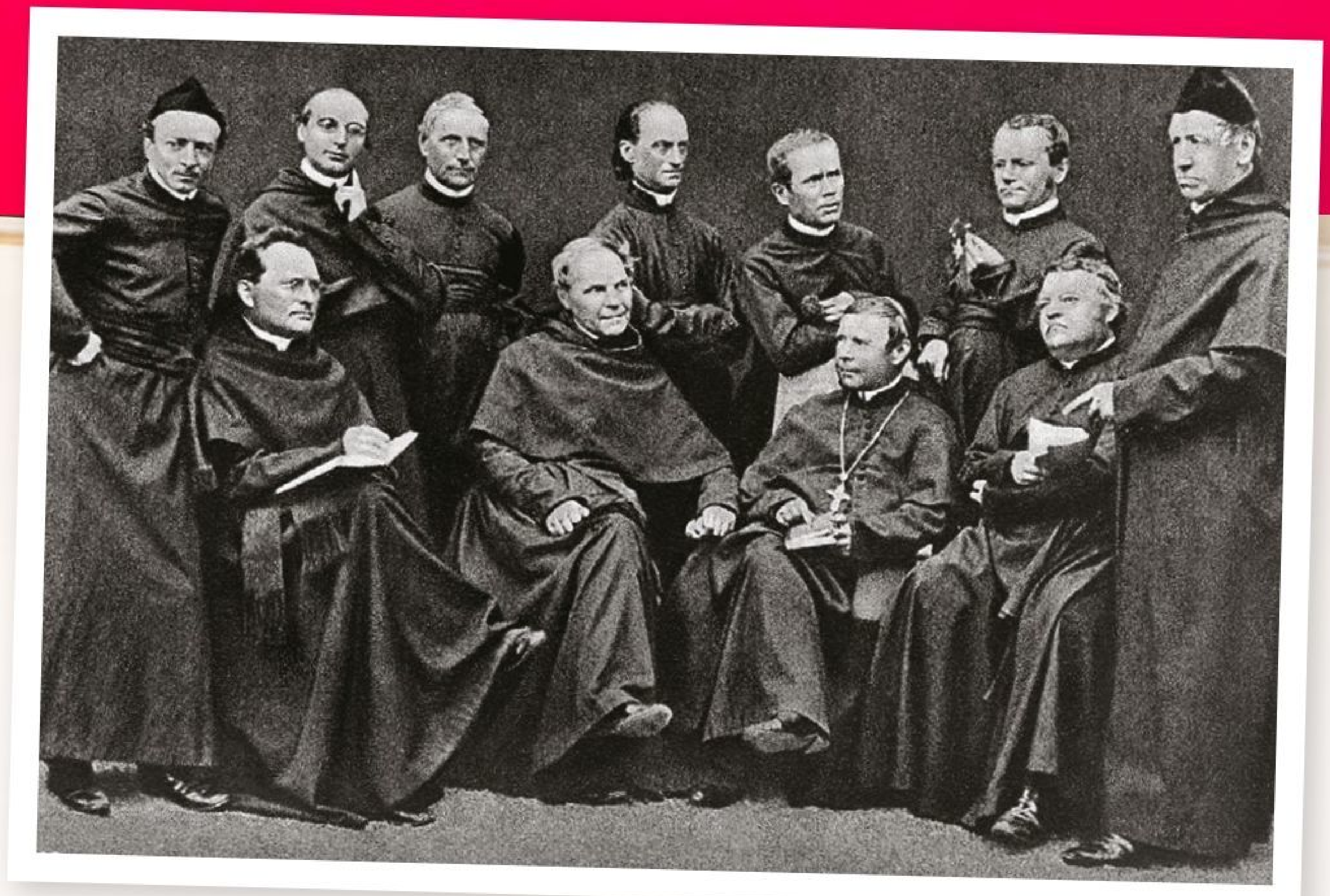
© Illustrations: Ed Crooks; Alamy; NASA

MENDEL'S PEAS

CZECH REPUBLIC, 19TH CENTURY

How do we inherit our genes from our parents? The answer was actually discovered not by studying humans but peas. Gregor Johann Mendel, an Augustinian friar, crossbred peas with differing characteristics in order to evaluate how different features were inherited in their offspring. His work focused on pea plants and their seven observable traits: the shapes of the pods and seeds; plant height; flower position; and seed, pod and flower colour.

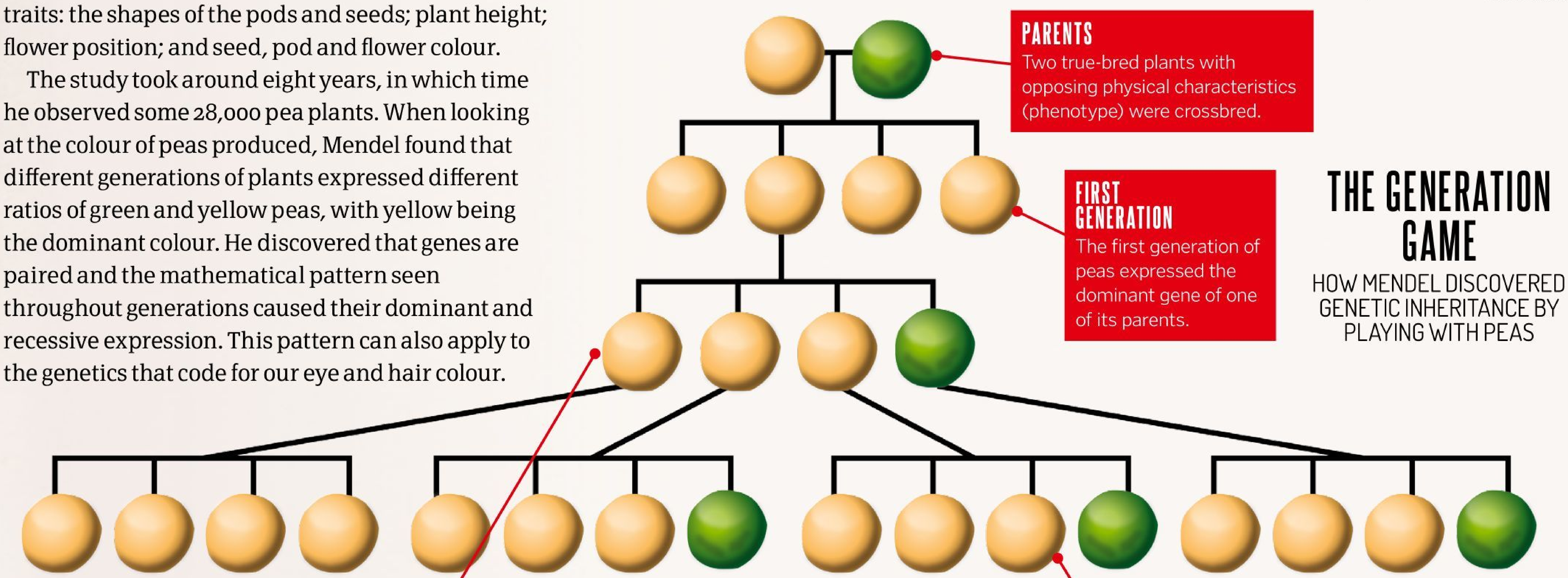
The study took around eight years, in which time he observed some 28,000 pea plants. When looking at the colour of peas produced, Mendel found that different generations of plants expressed different ratios of green and yellow peas, with yellow being the dominant colour. He discovered that genes are paired and the mathematical pattern seen throughout generations caused their dominant and recessive expression. This pattern can also apply to the genetics that code for our eye and hair colour.



○ Mendel (back row, right-hand side) pictured here with his fellow monks

THE GENERATION GAME

HOW MENDEL DISCOVERED GENETIC INHERITANCE BY PLAYING WITH PEAS



PARENTS
Two true-bred plants with opposing physical characteristics (phenotype) were crossbred.

FIRST GENERATION
The first generation of peas expressed the dominant gene of one of its parents.

SECOND GENERATION
This set of peas displayed a ratio of 3:1, three showing the dominant gene and one expressing the recessive gene.

SELF-POLLINATION
After the initial crossbreeding, peas were left to self-pollinate in order to explore a single lineage of genetics.

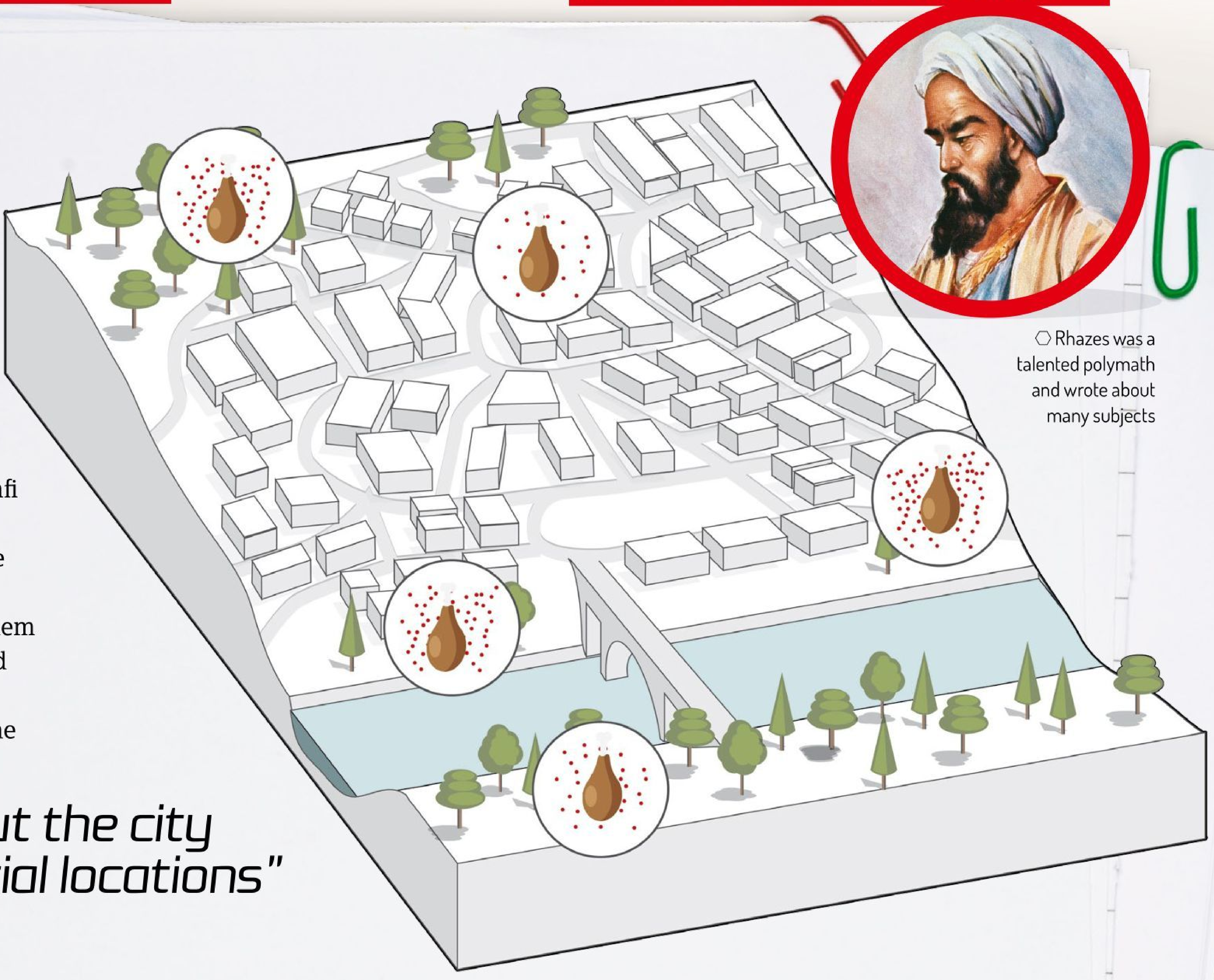
RHAZES AND THE HOSPITAL TRIAL

IRAQ, 10TH CENTURY

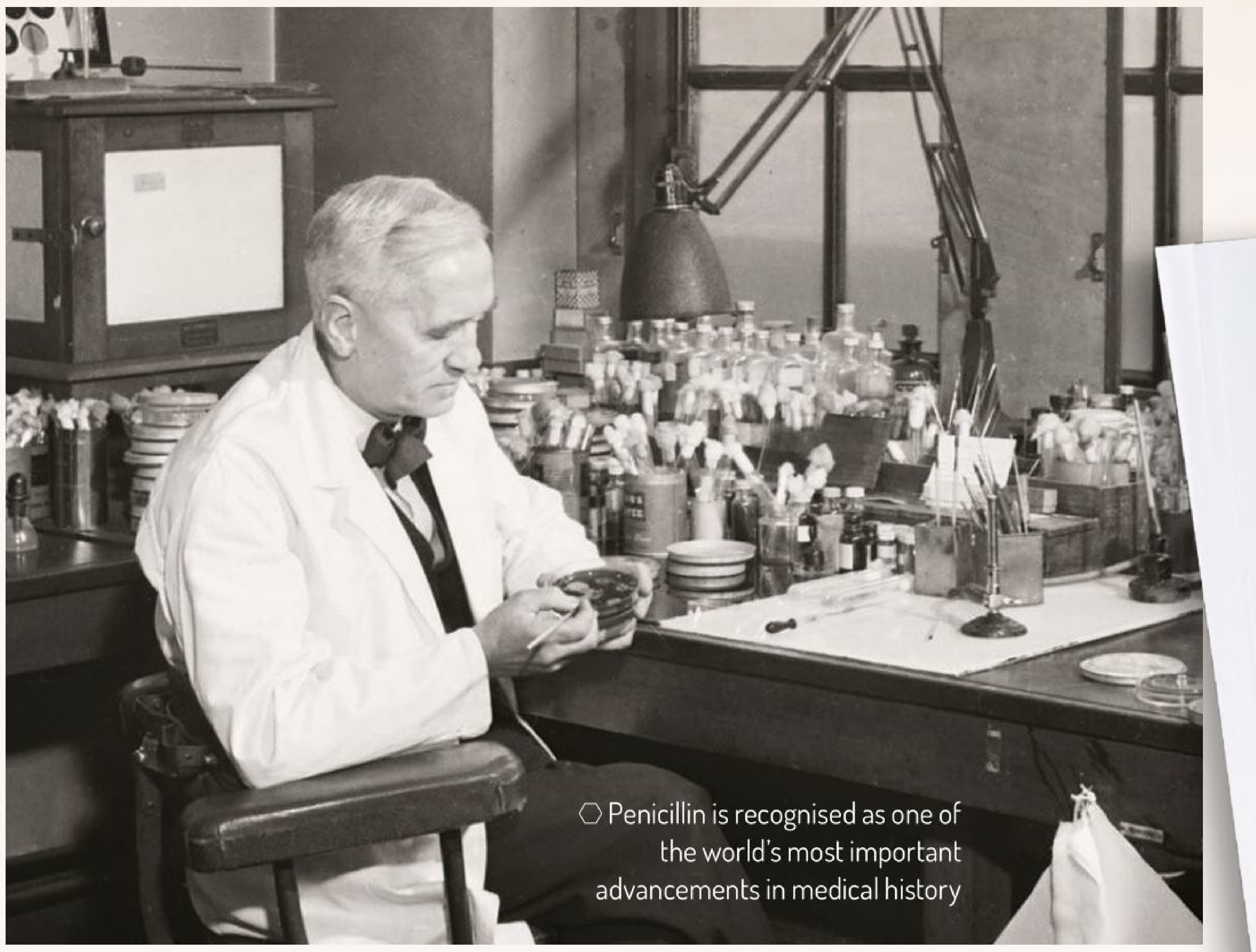
Abu Bakr Muhammad ibn Zakariya al-Razi, known as Rhazes in the West, was a physician of many talents, including his novel approach in determining the location of a Baghdad hospital.

Under the instruction of the Caliph al-Muktafi to determine where the city's newest hospital should be built, Rhazes used meat to select the right spot. He travelled throughout the city hanging meat in potential locations and left them for a few days. The place in which the meat had experienced the least amount of decay was selected to be the location for the hospital, as he deduced that this was the cleanest area.

○ Rhazes was a talented polymath and wrote about many subjects



"He travelled throughout the city hanging meat in potential locations"



Penicillin is recognised as one of the world's most important advancements in medical history

FLEMING'S ACCIDENTAL DISCOVERY OF PENICILLIN

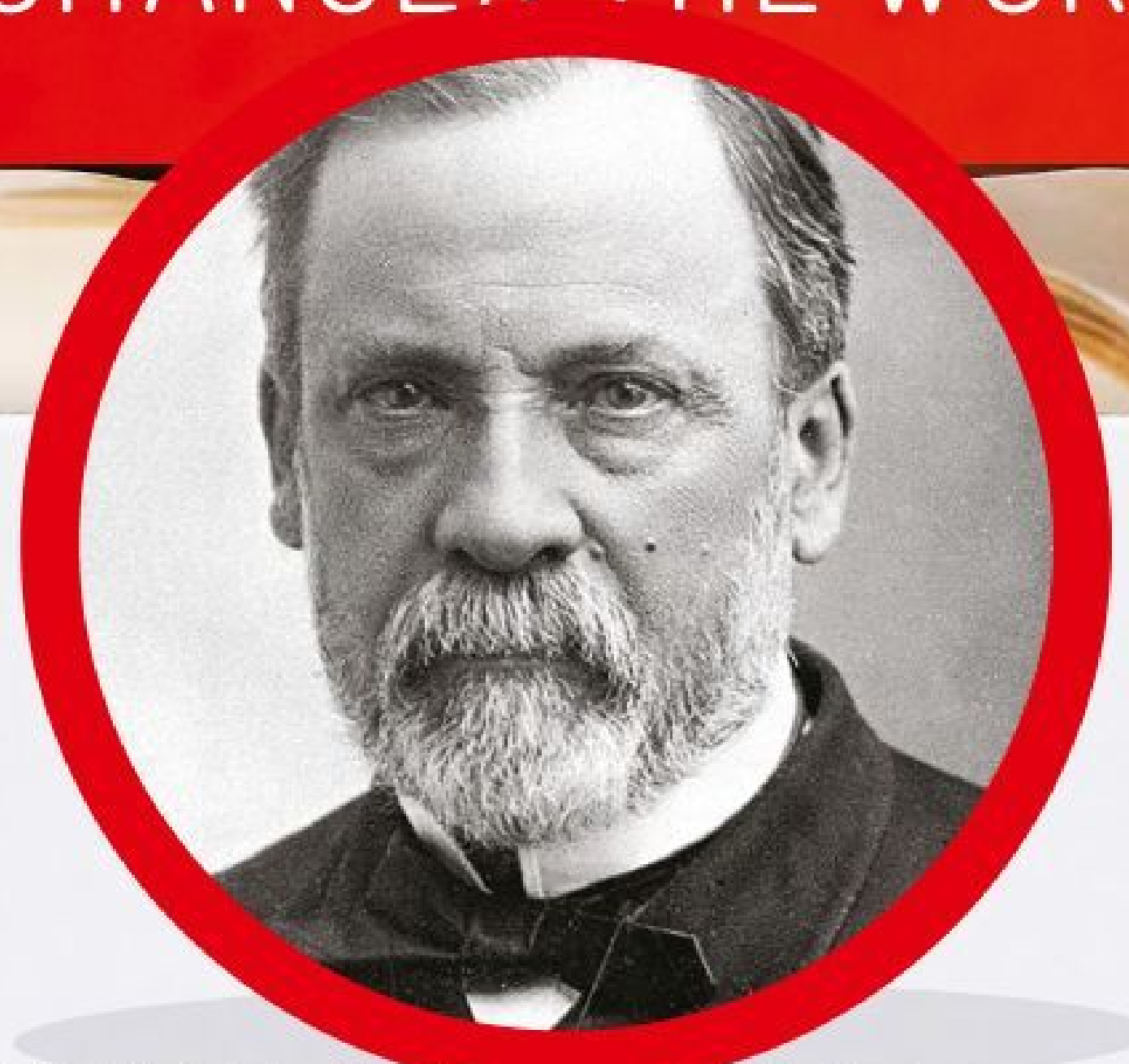
ENGLAND, 20TH CENTURY

In 1928, at St Mary's Hospital in London, Alexander Fleming was busy investigating the bacterium, *Staphylococcus aureus*. The bacteria had been wreaking havoc by causing fatal infections, and there was no medicine at the time to treat them.

On one occasion, Fleming forgot to put one of his Petri dishes into an incubator. While he was away on a two-week holiday the bacteria multiplied, and on his return he noticed something unusual in the rogue Petri dish. There was an area where the bacteria could not grow, and instead left a 'mould juice' to form a clear zone around itself. He investigated and found that the mould *Penicillium notatum* had contaminated the dish, inhibiting the growth of the bacteria.

In the late 1930s, scientists Howard Florey and Ernst Boris Chain managed to isolate and purify penicillin, and the antibiotic was available as an injection by 1941. It is estimated that this discovery has saved up to 200 million lives to date.

The use of penicillin during WW2 helped to save countless lives



PASTEUR UNCOVERS THE ORIGIN OF CELLS

FRANCE, 19TH CENTURY

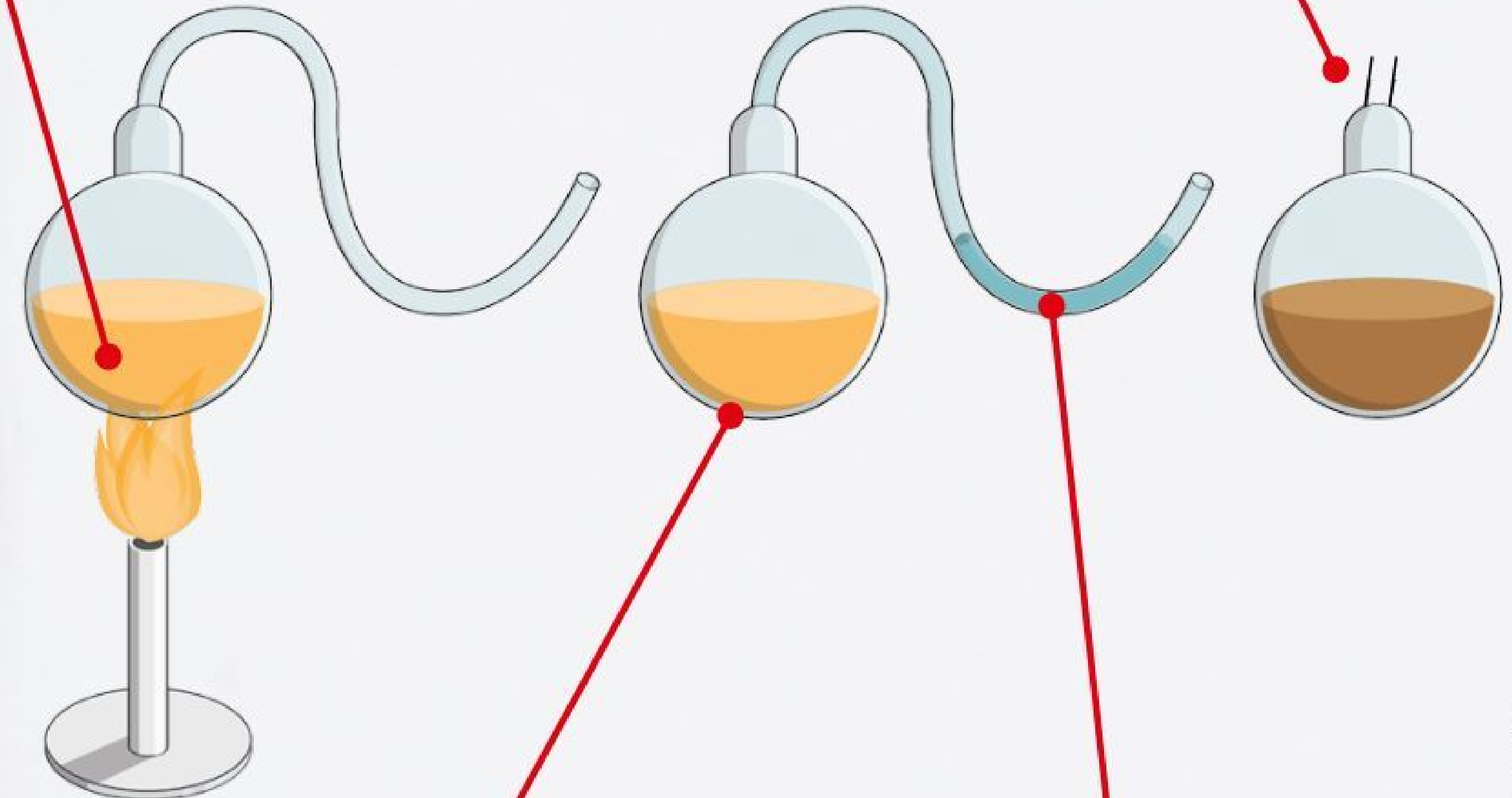
Back in the 1800s, people thought that spoiled food and diseases were caused by 'bad air' or life spontaneously generating. Louis Pasteur didn't – he rejected the idea that mice could be randomly created from rotting wheat and old cloth over a few weeks.

After noticing that his own vats of beer were turning sour, Pasteur started analysing them only to discover they were swarming with bacteria. This convinced him that the spoiling of his brew was caused by these tiny microorganisms. He designed a simple experiment to prove his revolutionary germ theory and as a result disproved the idea that cells could come from nothing.

So crucial was his work in the food and medicine industry that we even named a process after him: pasteurisation – the process of heat-treating something for a short time and cooling it down quickly to make it safe from bacteria.

MICROBE MATTERS

ARMED WITH A SET OF SWAN-NECK FLASKS, LOUIS PASTEUR SET OUT TO CHALLENGE THE STATUS QUO



THE EXPERIMENT
Two swan-neck flasks containing liquids filled with nutrients were boiled to sterilise the liquid.

STRAIGHT-NECK FLASK
The open flask allowed air and any bacteria to enter easily. The flask became murky with microbes growing in the liquid.

SUCCESS
Pasteur had proved that the organisms were not being spontaneously generated and that it was the result of germs getting into the flask that caused the liquid to go off.

S-SHAPED FLASK
The flask's swan-neck shape meant that condensed liquid pooled in the bend, creating a seal so germs could not enter. The liquid did not change colour or become cloudy.

© Illustrations: Ed Crooks; Wiki/Wellcome Collection

MARCONI'S WIRELESS REVOLUTION

ENGLAND, 20TH CENTURY

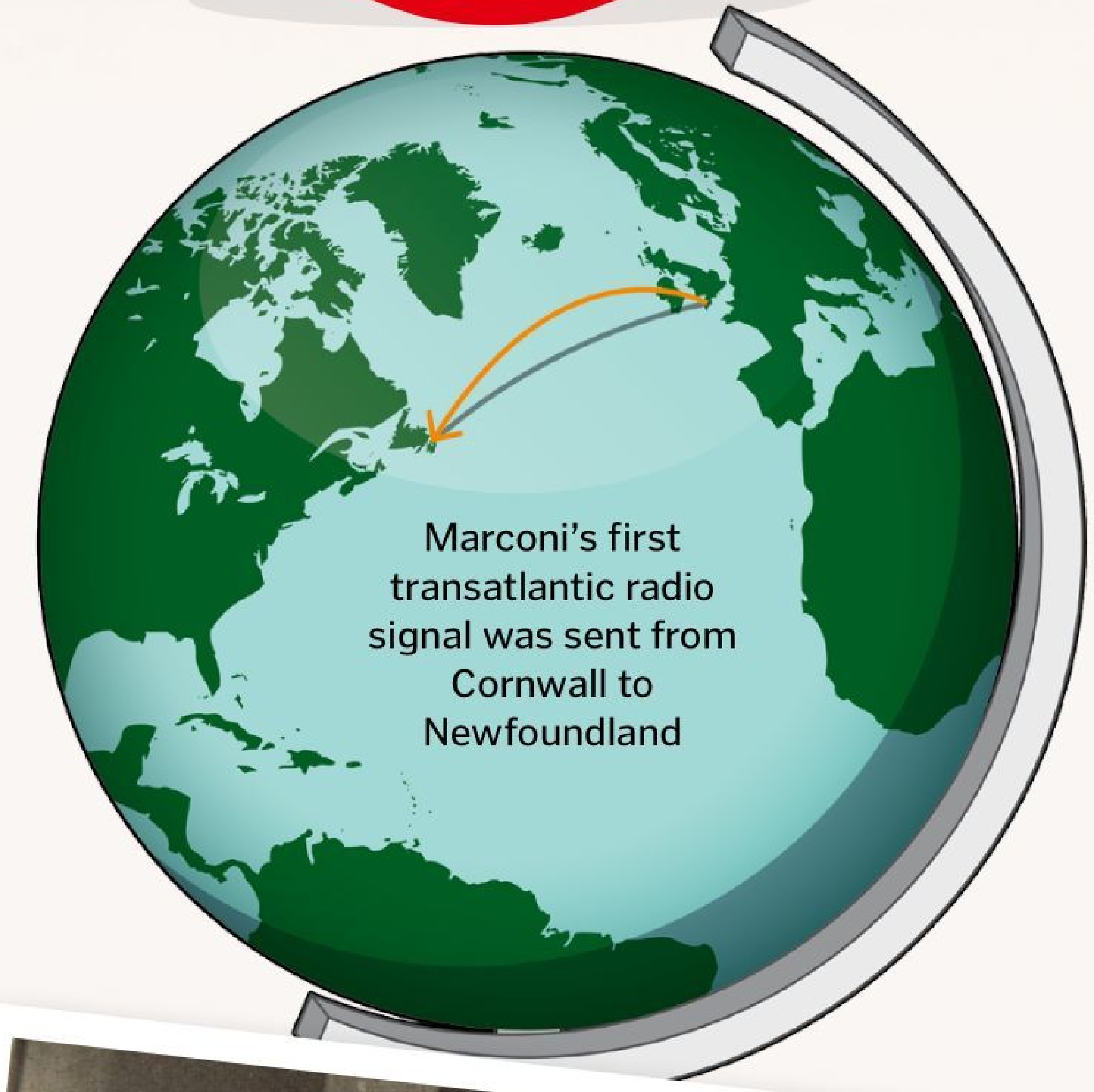
We live in a world where we can communicate with almost anyone, anywhere. Amazingly, to do this we don't need to be plugged in. Wireless communication has changed the world.

Italian physicist Guglielmo Marconi was a pioneer in telecommunications; influenced by the recent discovery of electromagnetic waves, at the age of just 20 he successfully transmitted a wireless signal over a distance of more than 2.4 kilometres. He was fanatical about invention and wanted to create something practical and commercially successful from this technology.

In 1897, he took to the Salisbury Plains to pitch his workable system to the British Government, which involved using an aerial held up by a balloon to improve the range of wireless transmission. When a Morse key was depressed it would cause a spark, which flowed up the antenna and radiated in all directions into space. As it spread through the air a second aerial connected to the receiver would pass over the coherer to complete the circuit and trigger a bell. He demonstrated that he could transmit this signal further than ever before without the need for wires. His next mission was to transmit over open sea, and he selected Lavernock Point, Wales, as the site of the momentous experiment.

Marconi continued to develop the technology, and on 12 December, 1901, he sent the first long-range radio message some 3,380 kilometres across the Atlantic, between Poldhu, Cornwall, England, and St John's, Newfoundland, Canada. The basis of all radio communication today had been invented, and though the equipment he used was not new, its organisation was.

"From my earliest experiments I had always held a belief that the day would come when mankind would be able to send messages without wires from between the further most ends of the Earth." How right Marconi was.



Marconi's first transatlantic radio signal was sent from Cornwall to Newfoundland

○ Much of the technology we take for granted today only exists because of Marconi's work

FERMI'S NUCLEAR REACTOR

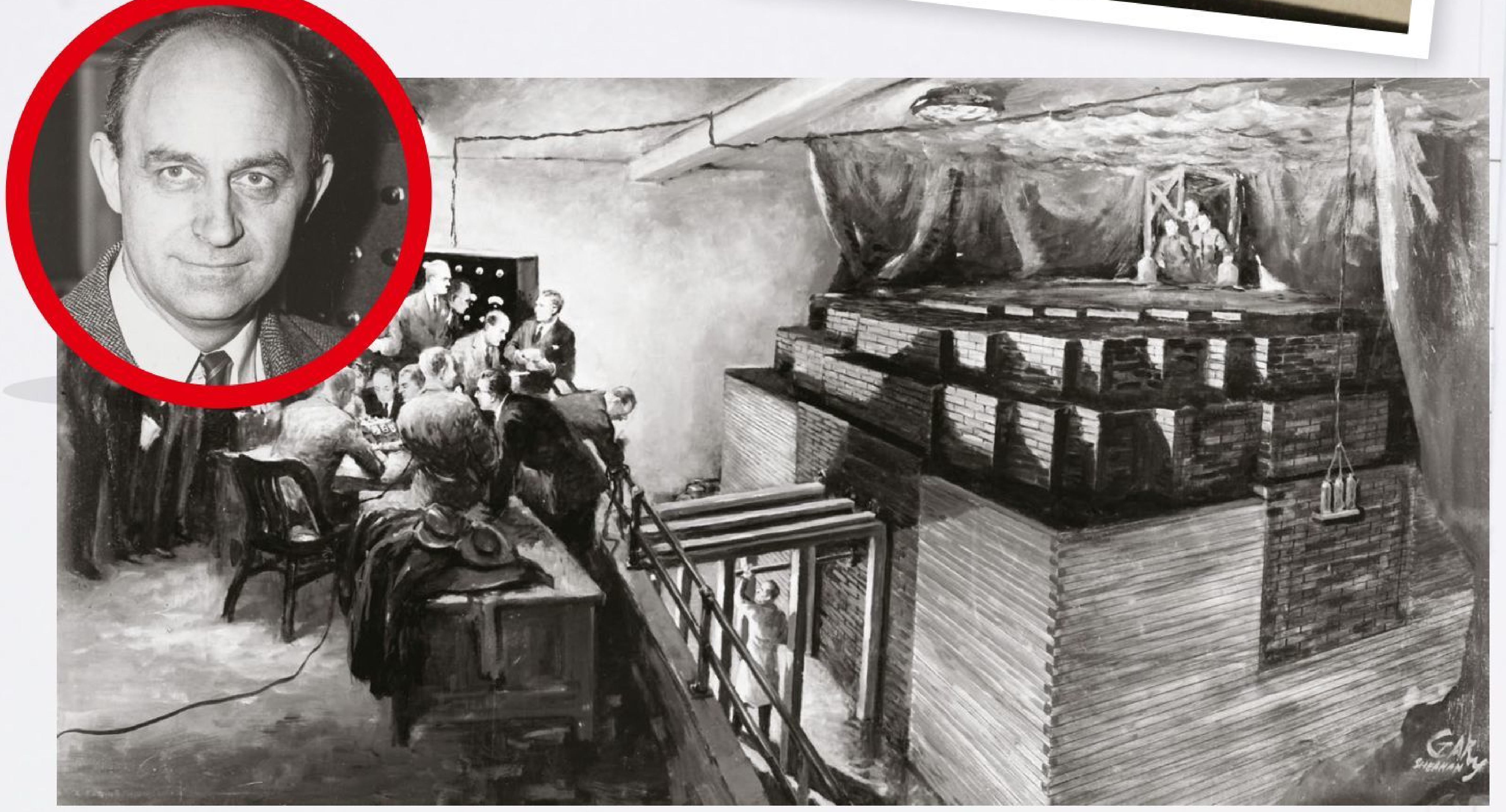
US, 20TH CENTURY

After the atom was split and the term 'nuclear fission' was coined, physicist Enrico Fermi applied the principle to create the first self-sustaining nuclear chain reaction in a human-made reactor: Chicago Pile-1.

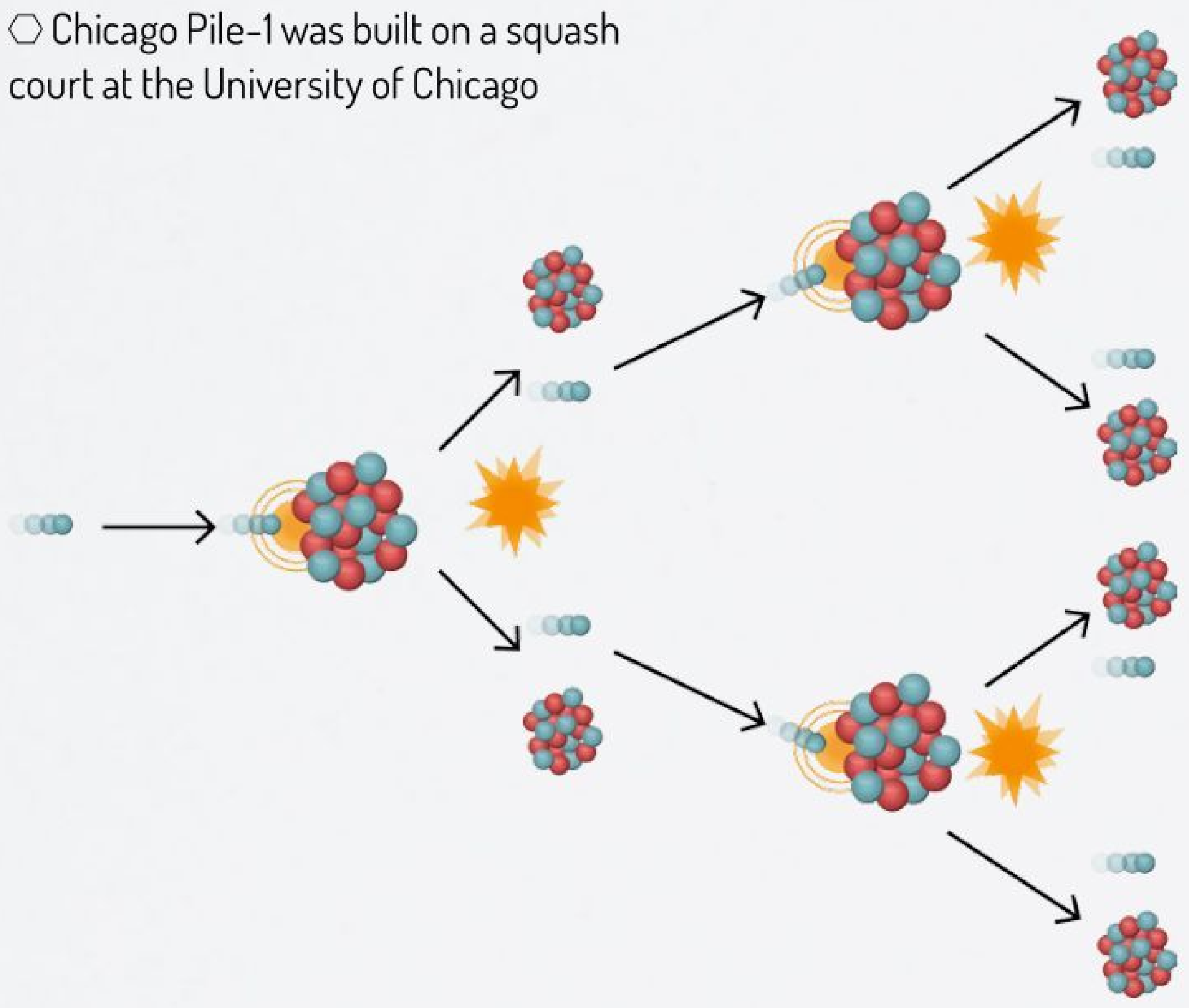
Scientists were aware that a nuclear reactor would allow for the production of a weapon like nothing seen before. The outbreak of WWII meant that weapon production was a priority, a consequence of which was the birth of both the Manhattan Project and Fermi's reactor.

Once uranium-235 is hit with a neutron the nucleus splits to form two smaller nuclei and more neutrons, which then go on to split other uranium atoms, thus forming a chain reaction. The reactor was made from stacks of graphite blocks to slow down fast uranium neutrons, increasing the likelihood of nuclear fission.

This reaction needed to be controlled in order for it to be safe. Control rods made from cadmium were used to absorb the excess neutrons created from the nuclear fission. Adding or removing the rods could control the longevity of the chain reaction. This reaction produced large amounts of energy, which could then be harnessed for warfare.



○ Chicago Pile-1 was built on a squash court at the University of Chicago



"Once uranium-235 is hit with a neutron, the nucleus splits to form two smaller nuclei and more neutrons"

RUTHERFORD STRIKES GOLD

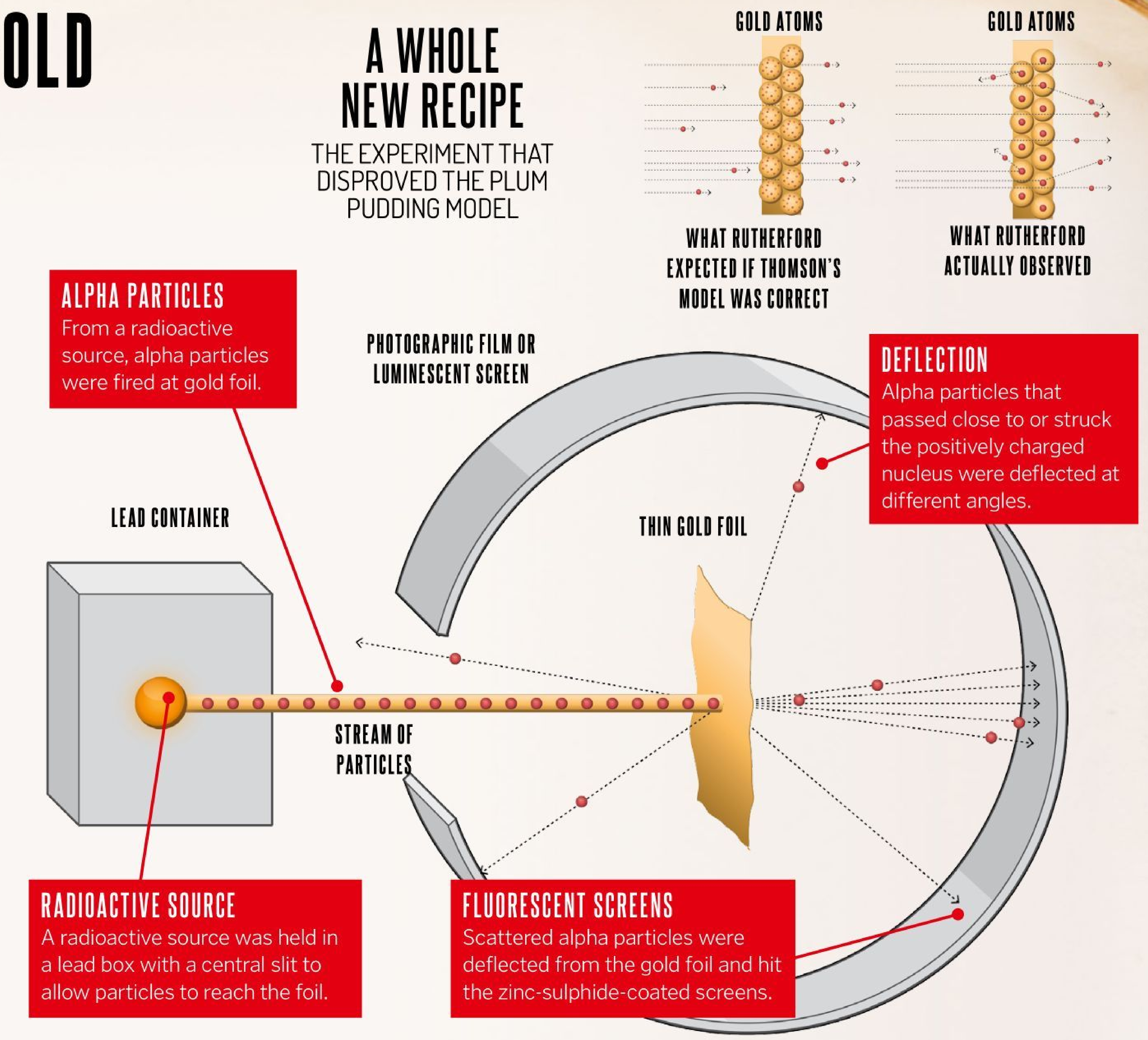
ENGLAND, 20TH CENTURY

It was previously believed that the structure of the atom was a sphere of positive charge housing smaller negatively charged electrons within it, like plums within a pudding. To test the accuracy of this 'plum pudding' model – under the direction of Ernest Rutherford – Hans Geiger and Ernest Marsden performed a series of experiments between 1908–1913 to prove Rutherford's theory of an atomic model, which resembled planets orbiting the Sun.

The physicists used a radioactive substance to bombard a thin piece of gold foil with positively charged alpha particles. The majority of particles passed through the foil without any deflection, suggesting that atoms had a great deal of open space. However, some were deflected off the gold foil at different angles, which meant that those particular particles had hit something with the same charge. This meant that rather than a positive charge engulfing electrons, a smaller positive charge was held in the dense middle, thus heralding the discovery of the atomic nucleus.

A WHOLE NEW RECIPE

THE EXPERIMENT THAT DISPROVED THE PLUM PUDDING MODEL


GOLD ATOMS
WHAT RUTHERFORD EXPECTED IF THOMSON'S MODEL WAS CORRECT
GOLD ATOMS
WHAT RUTHERFORD ACTUALLY OBSERVED
PHOTOGRAPHIC FILM OR LUMINESCENT SCREEN
LEAD CONTAINER
THIN GOLD FOIL
STREAM OF PARTICLES

ALPHA PARTICLES From a radioactive source, alpha particles were fired at gold foil.

DEFLECTION Alpha particles that passed close to or struck the positively charged nucleus were deflected at different angles.

RADIOACTIVE SOURCE A radioactive source was held in a lead box with a central slit to allow particles to reach the foil.

FLUORESCENT SCREENS Scattered alpha particles were deflected from the gold foil and hit the zinc-sulphide-coated screens.

LAVOISIER AND THE CONSERVATION OF MASS

FRANCE, 18TH CENTURY

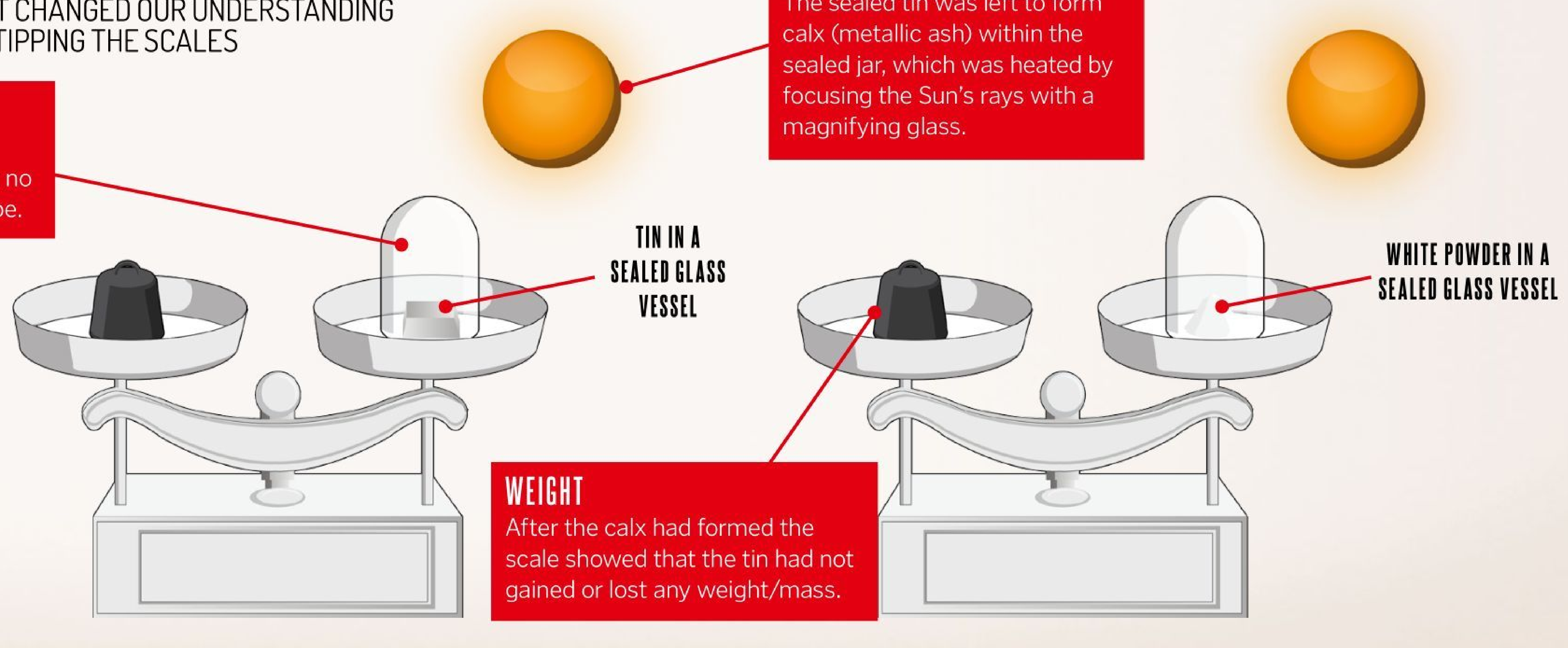
It was a French chemist named Antoine Lavoisier who formulated the concept of the conservation of mass – the idea that matter can neither be created nor destroyed, only rearranged. He did so by measuring the mass of reactants and products during chemical reactions.

One of Lavoisier's experiments entailed placing a burning candle inside a sealed glass jar. As the wick burned down and the candle melted the weight of the jar and its contents remained the same, thereby proving his pioneering theory.

At the time, chemists were exploring the formation of calx (an oxide), predicting that metals lost mass as they were burnt. Lavoisier countered this with the idea that calx was the result of atmospheric gas interacting with the metal. Rather than the metal losing mass, he found it gained weight by combining with oxygen from the air.

TRANSFORMING MATTER

THE EXPERIMENT THAT CHANGED OUR UNDERSTANDING OF MATTER WITHOUT TIPPING THE SCALES


TIN IN A SEALED GLASS VESSEL
WHITE POWDER IN A SEALED GLASS VESSEL

HEAT SOURCE The sealed tin was left to form calx (metallic ash) within the sealed jar, which was heated by focusing the Sun's rays with a magnifying glass.

SEALED JAR Tin was placed under a sealed jar to ensure that no gas could enter or escape.

WEIGHT After the calx had formed the scale showed that the tin had not gained or lost any weight/mass.

© Illustrations: Ed Crooks; Wiki; SPL

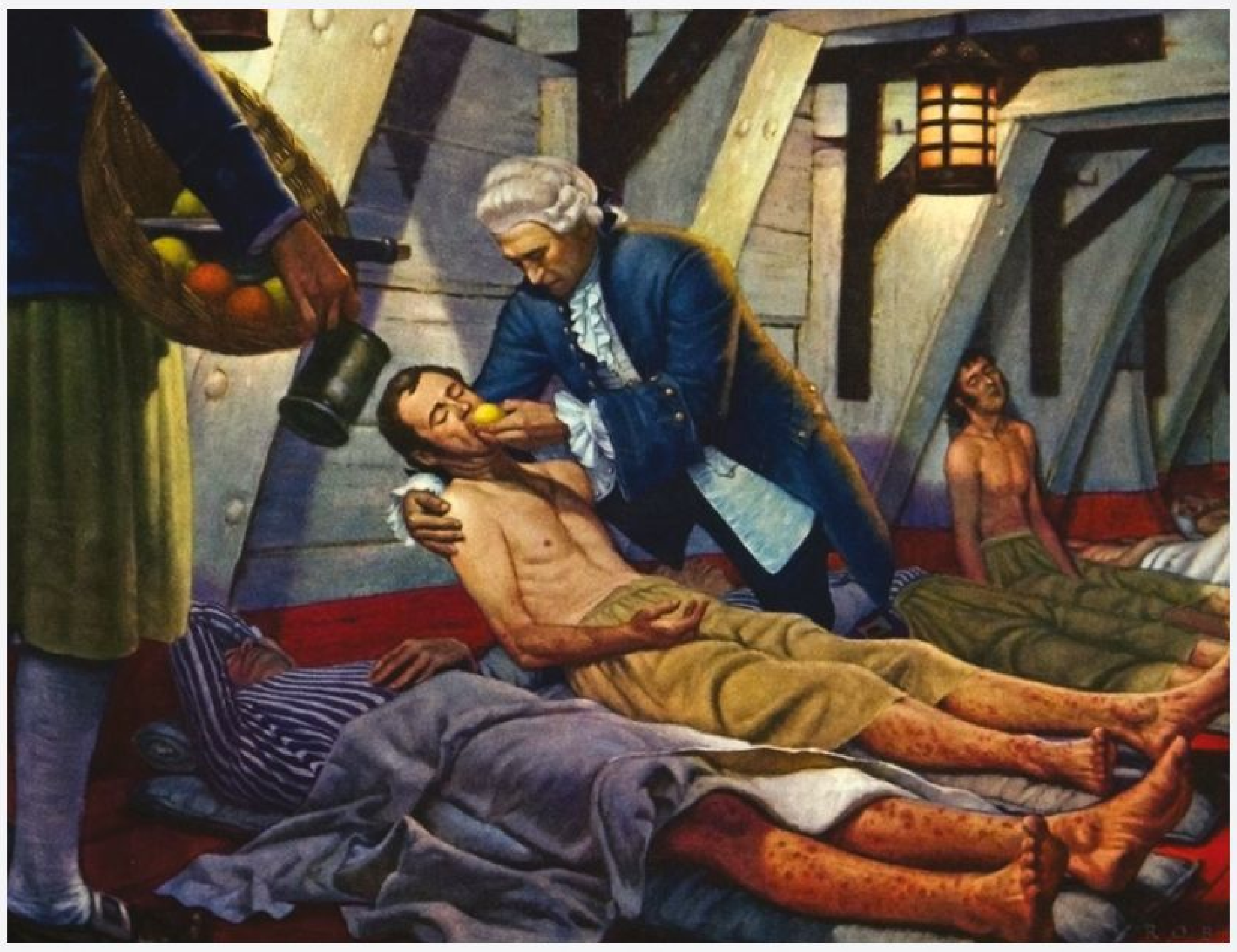
LIND CURES SAILORS' SCURVY

HMS SALISBURY, 18TH CENTURY

Bleeding gums, your teeth dropping out, weak limbs, swollen legs and nasty patches of blood under your skin – a pirate's life probably wouldn't have been ideal for most of us. Scurvy was one of the diseases that plagued pirates and sailors in the early days of seafaring. We know today that the disease is caused by a serious lack of vitamin C, something we need to form collagen, a vital component in structural and supportive connective tissue. Without enough collagen, the blood vessels and bones of those with scurvy break down until they suffer a slow and painful death. But in the time of Scottish physician James Lind, there was no knowledge about these tiny nutrients. People thought that scurvy might be contagious or caused by madness.

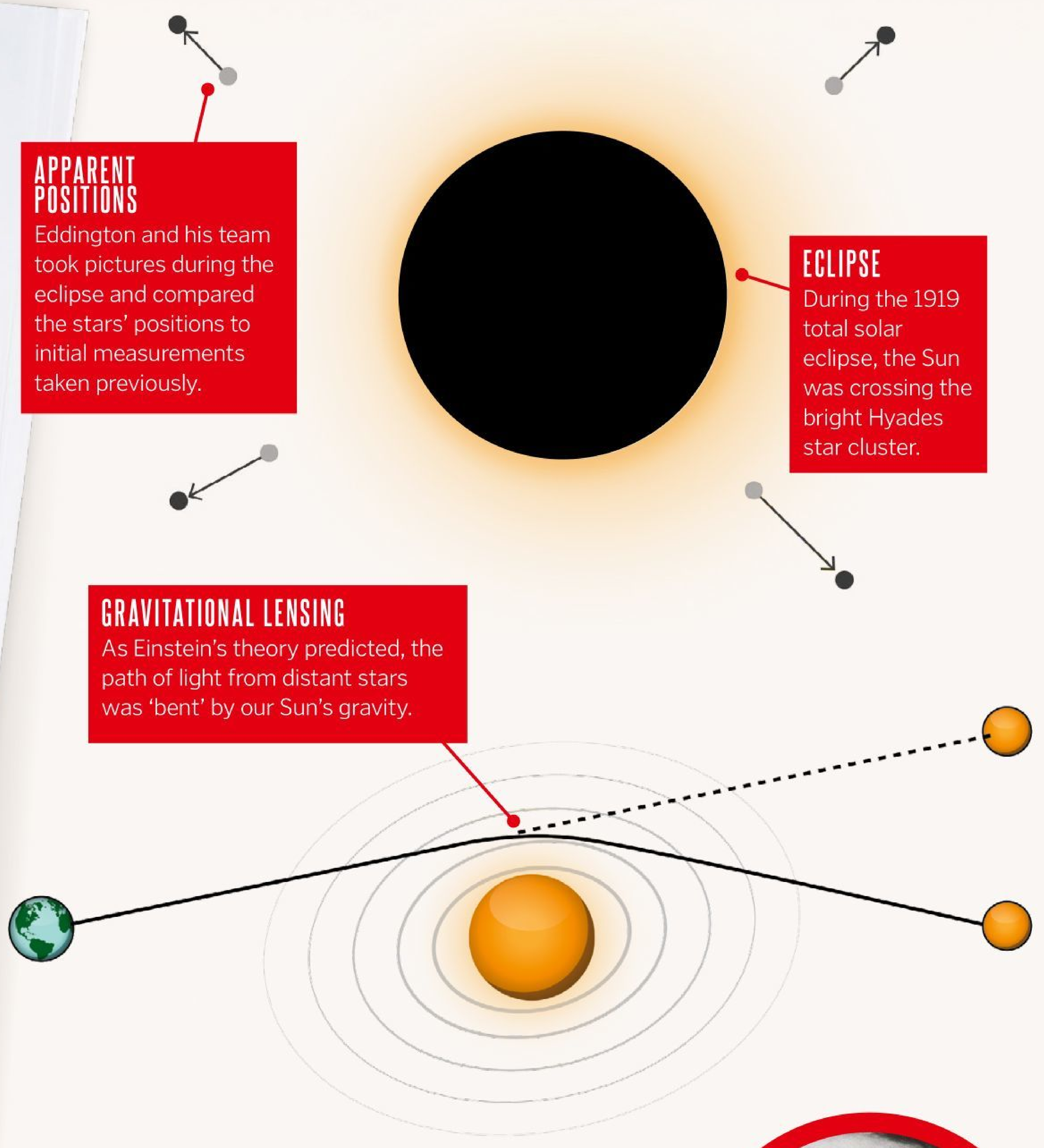
In 1747, Lind started one of the world's first clinical trials. He suspected that acids could help stop the putrefaction of the body, and he devised a trial to test different ways of introducing certain acids into people's diets. He divided a group of 12 scurvy-ridden sailors into six groups of two, all of which were to eat the same diet as one another but with the addition of an acidic supplement.

Each group was treated with either a quart of cider, 25 drops of elixir of vitriol, two spoonfuls of vinegar, half a pint of seawater, two oranges and one lemon, or a spice paste, every day. After six days most of the sailors eating the fruit had made an almost complete recovery. While Lind was on the wrong track about the cause of the disease, he had found the cure.



○ Scurvy is a disease that people around the world still suffer from, particularly in areas of war or famine

○ The solar eclipse allowed Eddington to observe how the light from stars is affected by the gravity of the Sun



APPARENT POSITIONS
Eddington and his team took pictures during the eclipse and compared the stars' positions to initial measurements taken previously.

ECLIPSE
During the 1919 total solar eclipse, the Sun was crossing the bright Hyades star cluster.

GRAVITATIONAL LENSING
As Einstein's theory predicted, the path of light from distant stars was 'bent' by our Sun's gravity.

EDDINGTON AND THE ECLIPSE

AFRICA, 20TH CENTURY

Scientific explanations in theoretical physics often remain just that, theoretical – but not all of them do. Albert Einstein published his general theory of relativity back in 1915, a criteria of which was that light bends near a massive gravitational force. However, Einstein was aware that should this or any of the other criteria required to support his revolutionary idea be disproven, then bang went the theory.

Einstein's pioneering work remained a theory until an astronomer named Sir Arthur Eddington used an eclipse to prove light could be bent by gravitational forces. In order for Einstein's theory to be correct, Eddington had to prove that the light had been bent by a source of intense gravity, such as the Sun. A total solar eclipse in 1919 presented Eddington with a unique opportunity to witness the night sky during the daytime.

After setting sail to Príncipe Island to get the best view of a predicted solar eclipse and test out Einstein's theory, Eddington observed the locations of stars at night and then again under the false night of an eclipse. This meant that he could observe if the gravity of the Sun had altered the stars' apparent positions, which in fact it had. This proved that light had been bent on its journey to Earth by way of the Sun's gravity, meaning Einstein was correct.

THE CREATION OF GRAPHENE

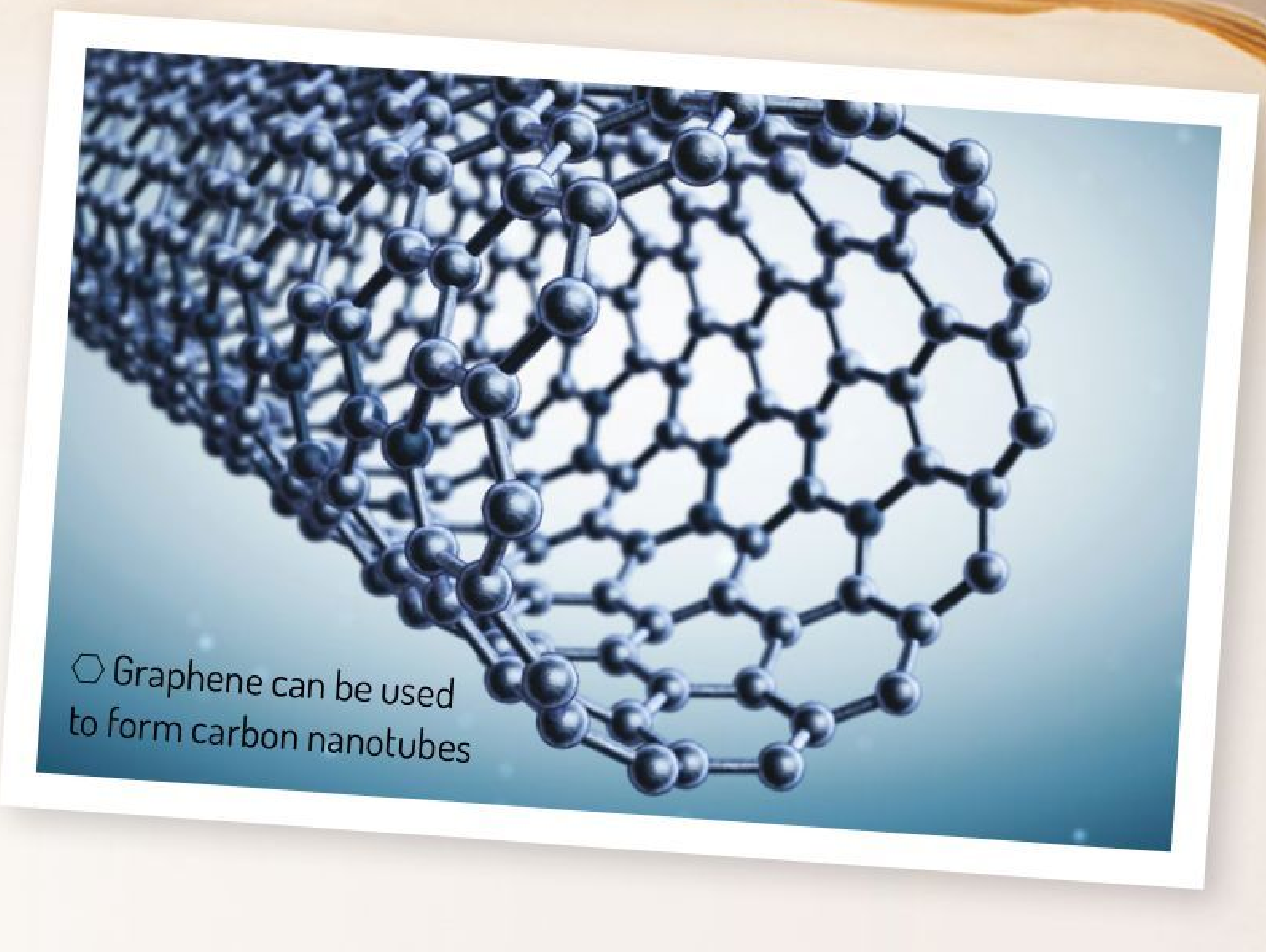
ENGLAND, 21ST CENTURY

In 2004, professors Andre Geim and Konstantin Novoselov were experimenting with a graphite crystal. They removed some graphite flakes using sticky tape and, upon closer inspection, realised that some of the flakes were thinner than others.

So they repeated the process, taking off more layers from the original peeled-off flake. Amazingly, their method worked. Each time the flakes were thinner, and they eventually managed to create flakes that were only one carbon atom thick. Although the existence of graphene had been predicted, no one knew how to isolate it. Until now.

It sounds simple, but graphene has turned out to be a really important material and just what we needed in this digital age for display screens and electric/photonic circuits. A fantastic conductor of heat, dense, lightweight, flexible and transparent, it has been used in everything from tyres to transistors.

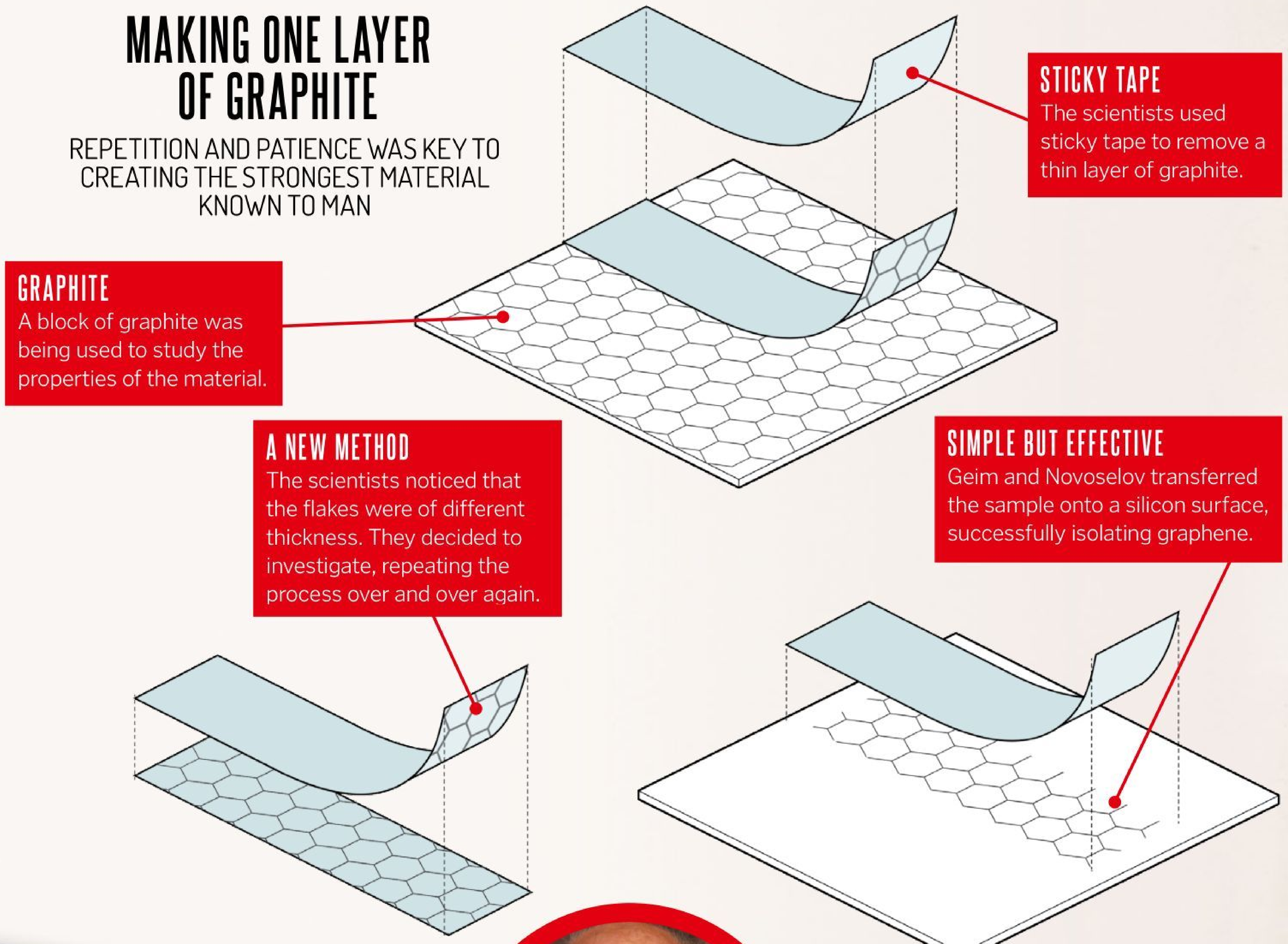
> *"Graphene has turned out to be a really important material in this digital age"*



○ Graphene can be used to form carbon nanotubes

MAKING ONE LAYER OF GRAPHITE

REPETITION AND PATIENCE WAS KEY TO CREATING THE STRONGEST MATERIAL KNOWN TO MAN



STICKY TAPE
The scientists used sticky tape to remove a thin layer of graphite.

GRAPHITE
A block of graphite was being used to study the properties of the material.

A NEW METHOD
The scientists noticed that the flakes were of different thickness. They decided to investigate, repeating the process over and over again.

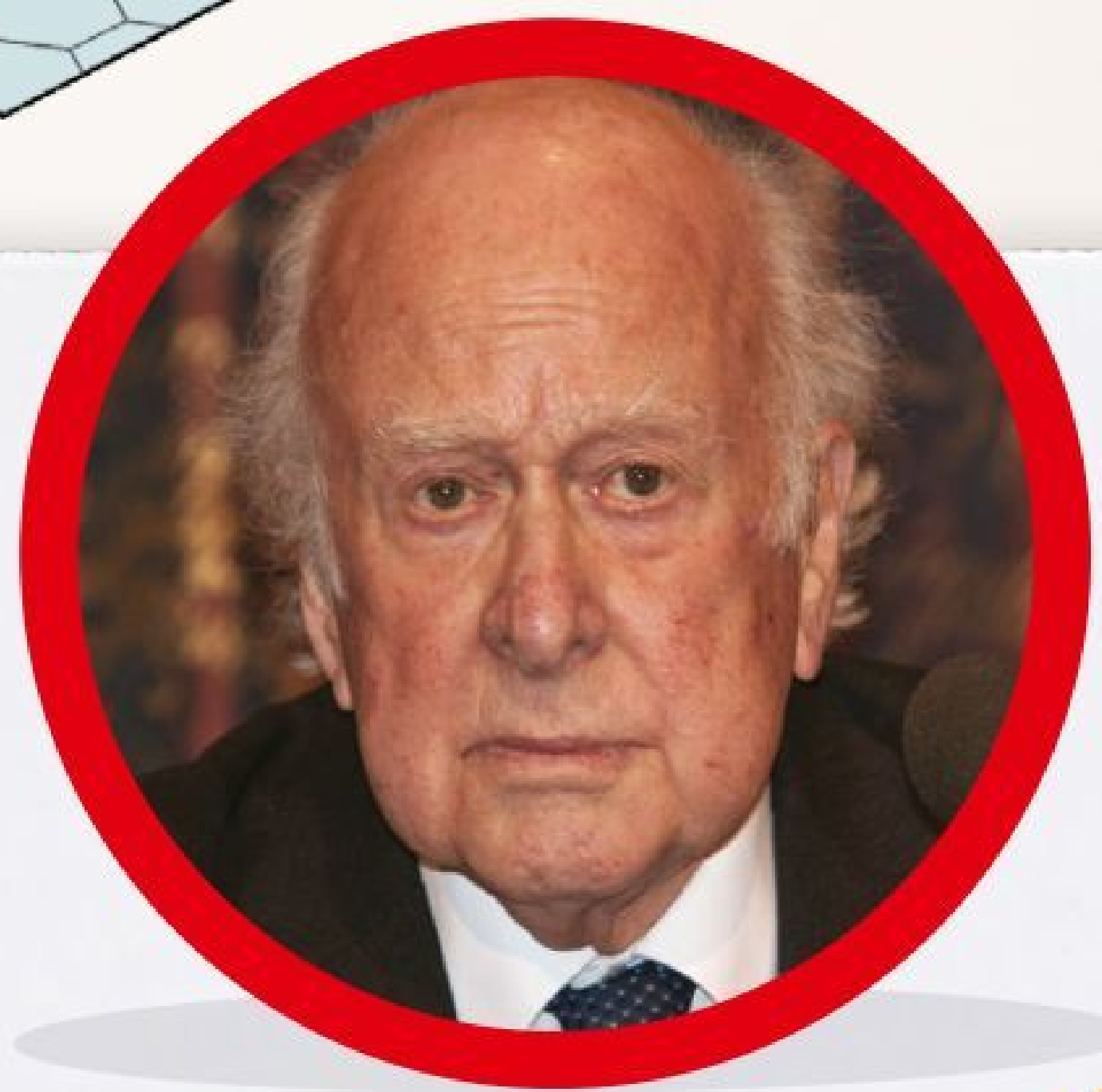
SIMPLE BUT EFFECTIVE
Geim and Novoselov transferred the sample onto a silicon surface, successfully isolating graphene.

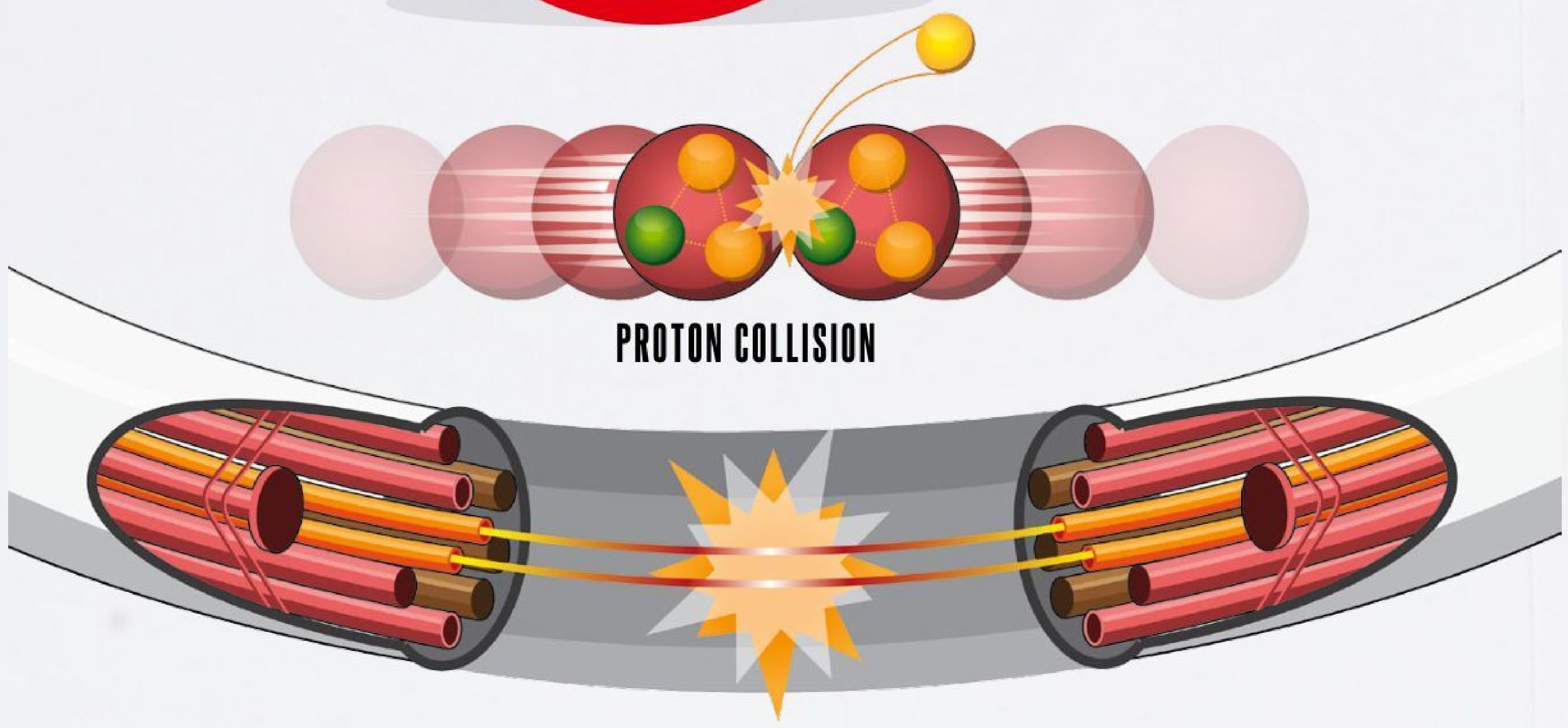
FROM THEORY TO REALITY

SWITZERLAND, 21ST CENTURY

In 1964, particle physicist Peter Higgs proposed a theory as to how particles have mass. He suggested that empty space is occupied by a field termed the Higgs field, where particles pass through it and either collect mass, like an electron, or don't interact with it at all and remain massless, such as a photon. An analogy would be a person moving through a crowd of strangers versus a crowd of friends.

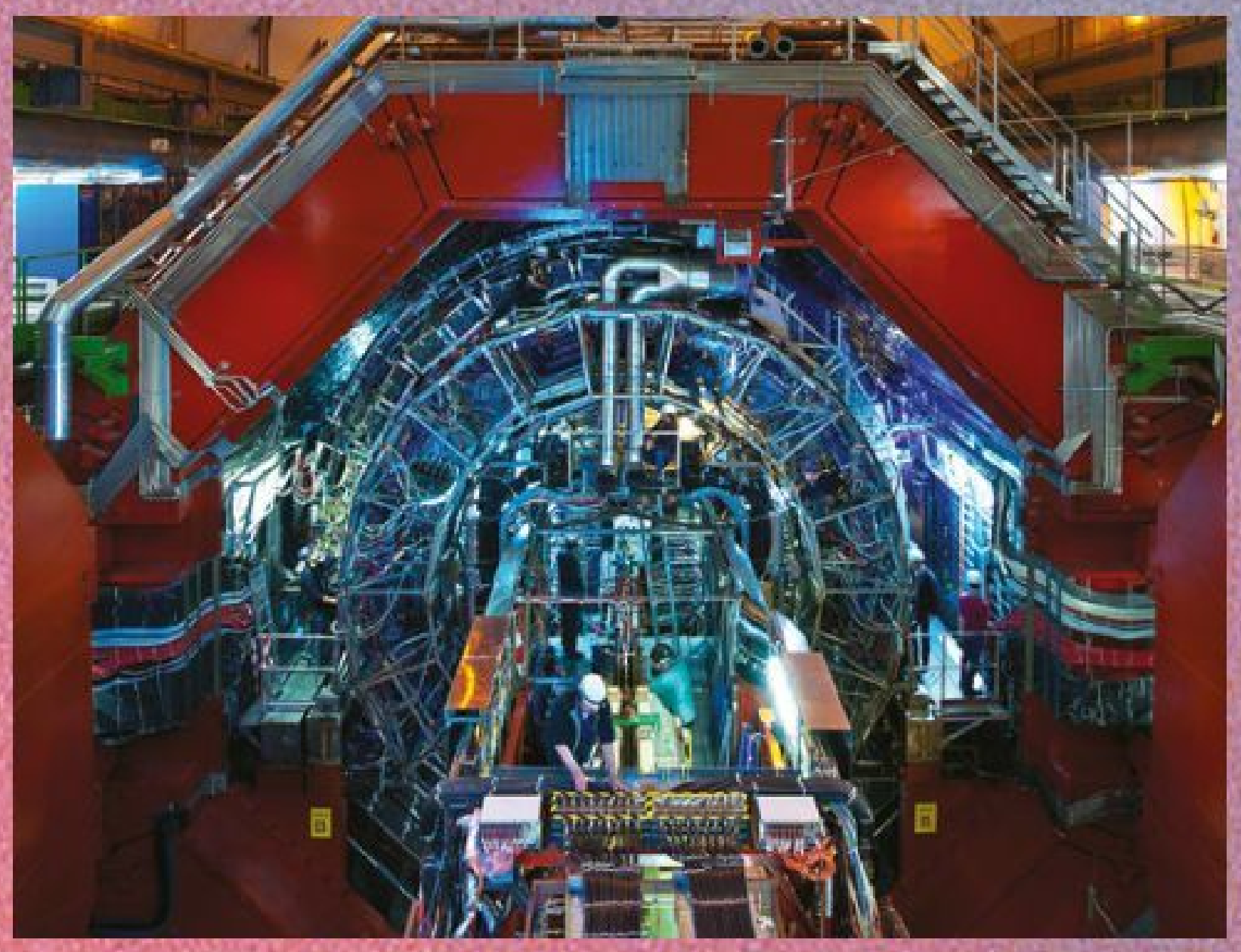
Moving through of crowd of strangers, you would pass easily without stopping, whereas if you were surrounded by friends you might stop to talk, thereby taking longer to make your way through. In this case your friends would be the Higgs boson. The Large Hadron Collider fires two beams of protons in opposite directions and accelerates them to near the speed of light so they collide to release the boson, something first acheived on 4 July 2012.





○ Higgs received the Nobel Prize in Physics in 2013 for his theoretical discovery

© Illustrations: Ed Crooks; Wiki/ cellan/ Dyor; Alamy

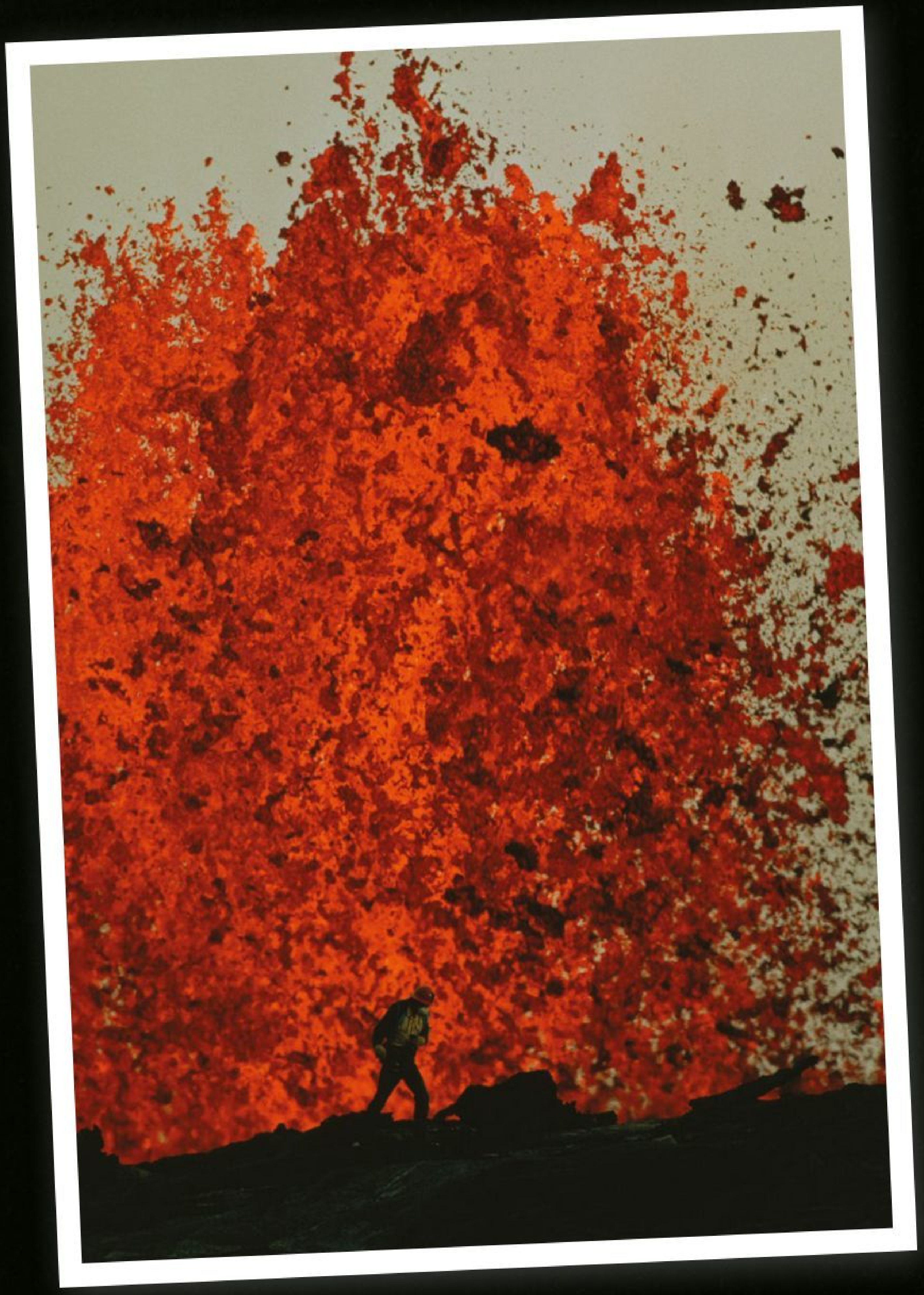


EXTREME SCIENCE

WELCOME TO THE MOST DANGEROUS AND REMOTE RESEARCH ON THE PLANET

> *“Volcanoes could explode at any moment, and volcanologists make it their business to explore them”*

Volcanologists get close to active volcanoes to collect samples and gather data



VOLCANOLOGY

THESE EXTREME SCIENTISTS GET UP CLOSE AND PERSONAL WITH ACTIVE VOLCANOES

Volcanoes are some of the most wild and extreme places on the planet. They sink right into the molten heart of the Earth, connecting the ground with the magma that is normally hidden beneath. Some could explode at any moment, and volcanologists make it their business to explore them.

Many different sciences come together to understand how volcanoes work and when and why they might erupt. Researchers need to know about the structure of the Earth, the chemistry of the rocks and how they interact with other chemicals in the air or water. They also need to understand the physics of our planet, and what drives movement deep beneath the surface.

Volcanologists travel all over the world in pursuit of active volcanoes, and live for a few months of the year out in the field. There's no denying that this type of work is dangerous. The temperature of lava varies depending on the volcano, but it can reach upwards of 1,000 degrees Celsius. They also produce deadly gases, including suffocating carbon dioxide, which collects in low-lying areas, and hydrogen sulphide, which has a strong smell of rotten egg, and can cause respiratory damage or even death. In 1991, the Unzen volcano erupted in Japan, killing volcanologists Maurice and Katia Krafft, and Harry Glicken.

But accidents like this are rare. A lot of work is done with dead or dormant volcanoes, and for most of the year, volcanologists work safely back at base, crunching their data, analysing samples, teaching and remotely monitoring volcanoes for signs of activity.

WHY THEY DO IT

TO PREDICT ERUPTIONS
Volcanoes are a threat to people, property and aircraft.

TO UNCOVER ANCIENT HISTORY
Mapping the history of eruptions can reveal the past.

TO LEARN ABOUT EARTH
Volcanoes can teach us what happens beneath the Earth.

© Getty; Alamy; WIKI; NASA

GOING UNDER

MEET THE RESEARCH TEAMS WORKING AT EXTREME DEPTHS

Most of the world's research labs sit at, or just above, ground level, but some enterprising teams have buried themselves deep below the Earth's surface.

Our planet is a noisy place; the Sun showers us with cosmic rays, communication towers spit out a constant stream of radio waves, and radioactive rocks and gases release a steady trickle of radiation. To get to grips with the particle physics that makes the universe go round, scientists need to block out this static so that they can examine the behaviour of particles in peace. To do this, they go underground.

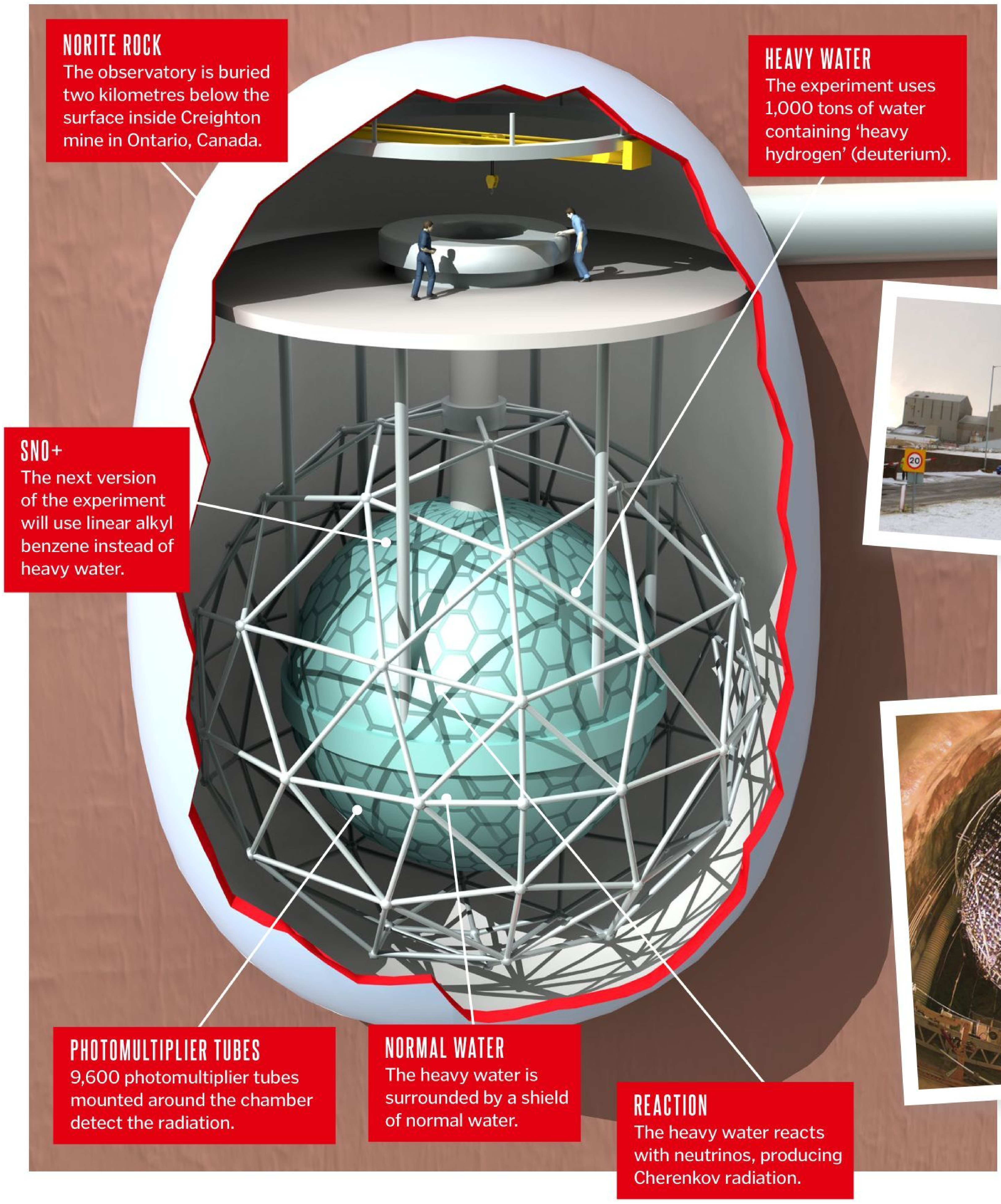
Muons are some of the most irritating particles, and constantly appear at Earth's surface as a result of cosmic rays. The further underground you go, the more are filtered out.

The deepest of these buried facilities is based in China, 2,400 metres below the mountain's surface. The China Jinping Underground Laboratory is hidden inside a mountain, and to add to its comic book credentials, the purpose of the lab is to search for dark matter.

This extreme research is at the cutting-edge of science, and it continues to produce exciting and groundbreaking physics again and again.

SNOLAB'S SNO EXPERIMENT EXPLORED

THE SUDBURY NEUTRINO OBSERVATORY DETECTS NEUTRINOS GENERATED IN THE HEART OF THE SUN



NORITE ROCK
The observatory is buried two kilometres below the surface inside Creighton mine in Ontario, Canada.

HEAVY WATER
The experiment uses 1,000 tons of water containing 'heavy hydrogen' (deuterium).

SNO+
The next version of the experiment will use linear alkyl benzene instead of heavy water.

PHOTOMULTIPLIER TUBES
9,600 photomultiplier tubes mounted around the chamber detect the radiation.

NORMAL WATER
The heavy water is surrounded by a shield of normal water.

REACTION
The heavy water reacts with neutrinos, producing Cherenkov radiation.

WHY THEY DO IT

TO LEARN ABOUT SUBATOMIC PARTICLES

Tiny particles can be examined in detail.

BECAUSE THE SURFACE IS NOISY

The Earth shields sensitive equipment from cosmic rays.

IT'S GROUNDBREAKING

Excuse the pun. Research in this field has won Nobel Prizes.

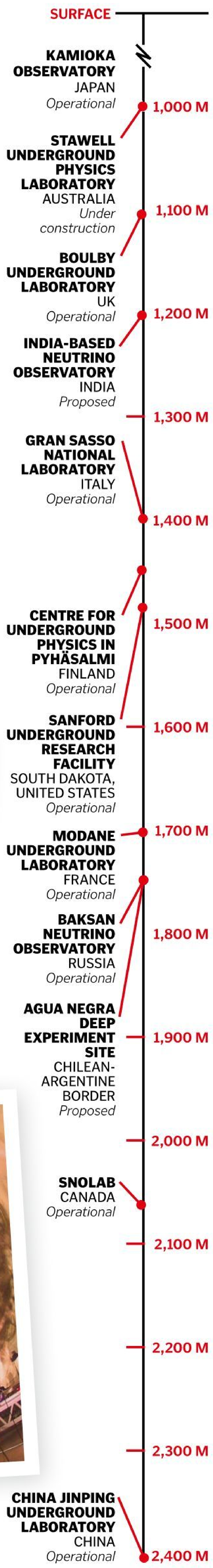
CLEVELAND POTASH
20
CPL are proud to host Boulby Underground Laboratory for Dark Matter Research

○ From the outside these labs look like any other, but underground they're at the forefront of physics

○ The SNOLAB SNO detector uses a sphere of heavy water to observe neutrinos

UNDERGROUND LABORATORIES

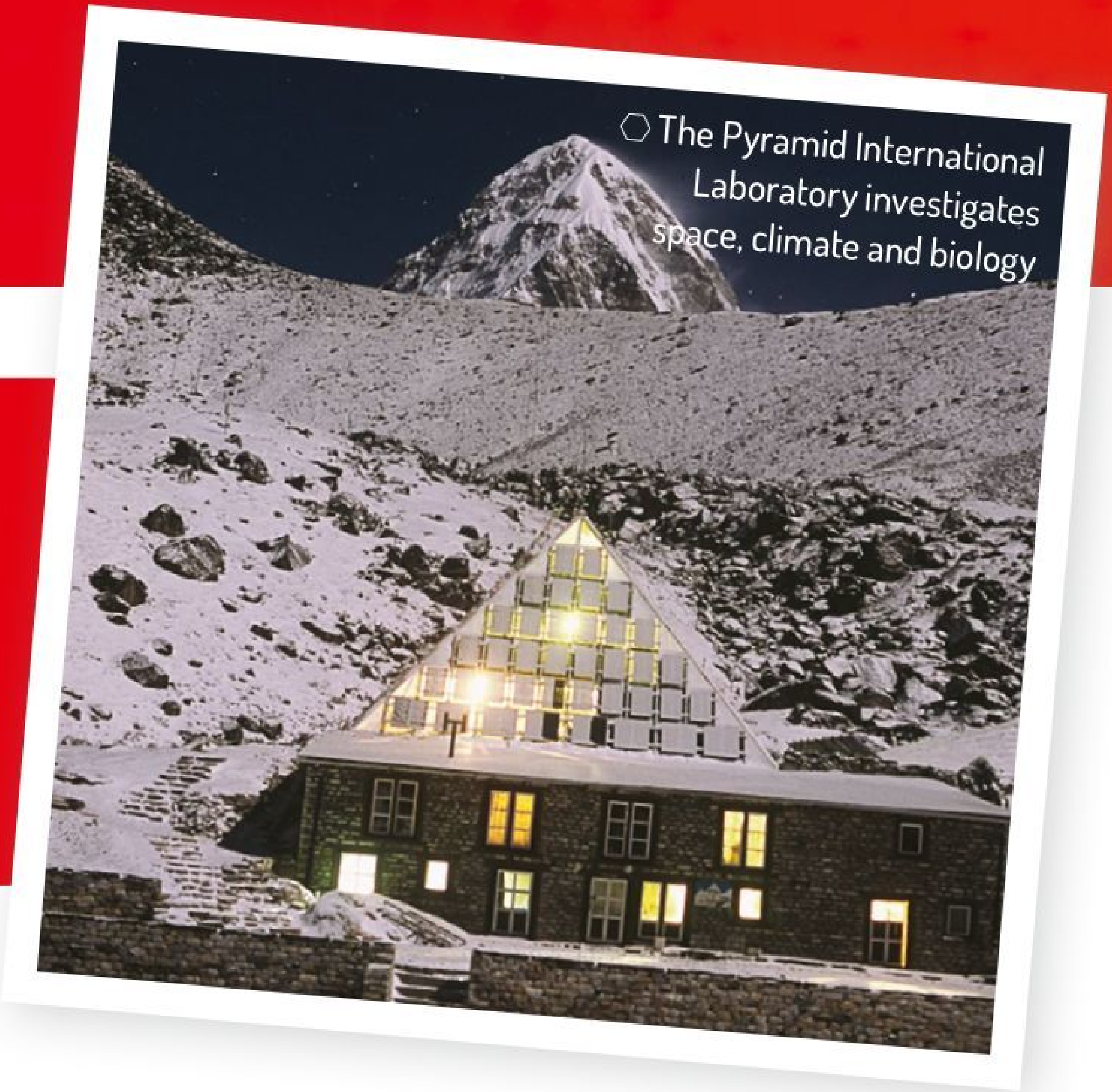
EXPERIMENTS DEEP BELOW THE GROUND



RESEARCH IN THE CLOUDS

The Pyramid International Laboratory/Observatory is perched among the mountains of the Himalayas, at the base of Mount Everest. Far from civilisation, the facility utilises renewable energy in the form of solar panels for energy, and relies heavily on food deliveries to keep its inhabitants well fed.

At just over 5,000 metres above sea level, it provides a unique environment for scientific studies. At this altitude, not only is the climate and environment different, the human body also behaves strangely, and there is a clearer line of sight into outer space.



○ The Pyramid International Laboratory investigates space, climate and biology

UNDER THE SEA

LIVING AND WORKING UNDERWATER IS MORE THAN JUST SCIENCE FICTION

The Florida Keys are home to the Aquarius Reef Base, a submerged laboratory run by Florida International University, which sits nearly 15 metres below the surface of the sea. At this depth, the pressure is around 2.5 times greater than it is on the surface. The lab sits next to one of the largest coral reefs in the world, providing a unique viewpoint to study these incredible ecosystems up close without the risk of disturbing them.

The base's inhabitants, known as 'aquanauts', train for five days before descending to the lab. They live at underwater pressure without returning to the surface for up to two weeks.

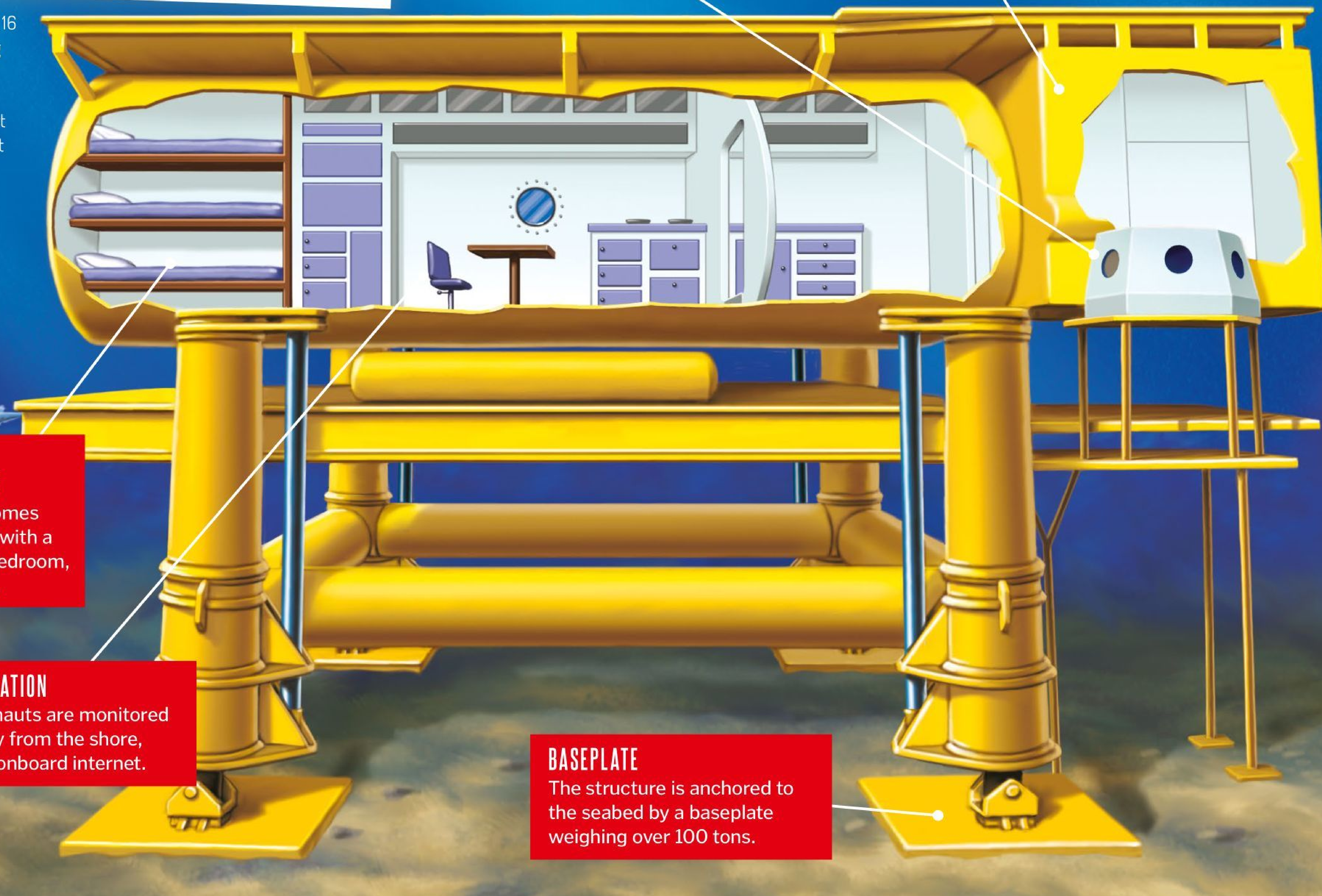
A floating life support system, complete with power generators, air compressors, and communications equipment, keeps them alive, and when it is time to come back again, the entire station decompresses slowly, allowing their bodies to adjust to normal air pressure before they swim back up.

Not only do scientists use the base to study the environment, space agencies send astronauts there for training and mission simulations.

○ The NEEMO 16 crew, including Tim Peake (upper left), prepare to start their mission at the Aquarius Reef Base

THAT SINKING FEELING

AQUANAUTS SPEND AROUND TEN DAYS AT A TIME LIVING ON AQUARIUS STATION



LIFE SUPPORT
A 9m-wide buoy floats above the station, providing power and compressed air.

WET PORCH
Aquanauts enter and exit through a 'moon pool' that is open to the water.

STEEL HABITAT
The lab and living space is 2.8m wide and 13m long.

ON-BOARD FACILITIES
The lab comes complete with a kitchen, bedroom, and toilet.

COMMUNICATION
The aquanauts are monitored constantly from the shore, and have onboard internet.

BASEPLATE
The structure is anchored to the seabed by a baseplate weighing over 100 tons.

© WIKI; SNOLAB_SNO; illustration by Adrian Mann;

LIFE ON THE ICE

HUNDREDS OF SCIENTISTS BRAVE ANTARCTIC ICE EACH YEAR TO EXPERIMENT IN THIS UNFORGIVING ENVIRONMENT

Antarctica is the only continent with no native human inhabitants and no permanent human residents, but visiting scientists make this isolated continent a temporary home. During the summer, a few thousand people arrive to begin their experiments, and in the depths of winter, a few hundred remain to keep the buildings and science ticking over until the place warms up again.

With average temperatures of -12 degrees Celsius at the coast and -60 degrees Celsius at high altitude, it's no wonder that the scientists don't remain all year round. Food and supplies can be delivered during the summer, but when winter hits the resupply stops. For some bases, this lack of fresh produce can last for ten months of the year, and the inhabitants must rely on frozen and canned stores.

Once these basic needs are taken care of, the stations are relatively safe places to stay; it's venturing out to perform experiments that poses the biggest danger. Research teams travel by sledge or air to key locations, and camp out in the wild until they have the data that they need.

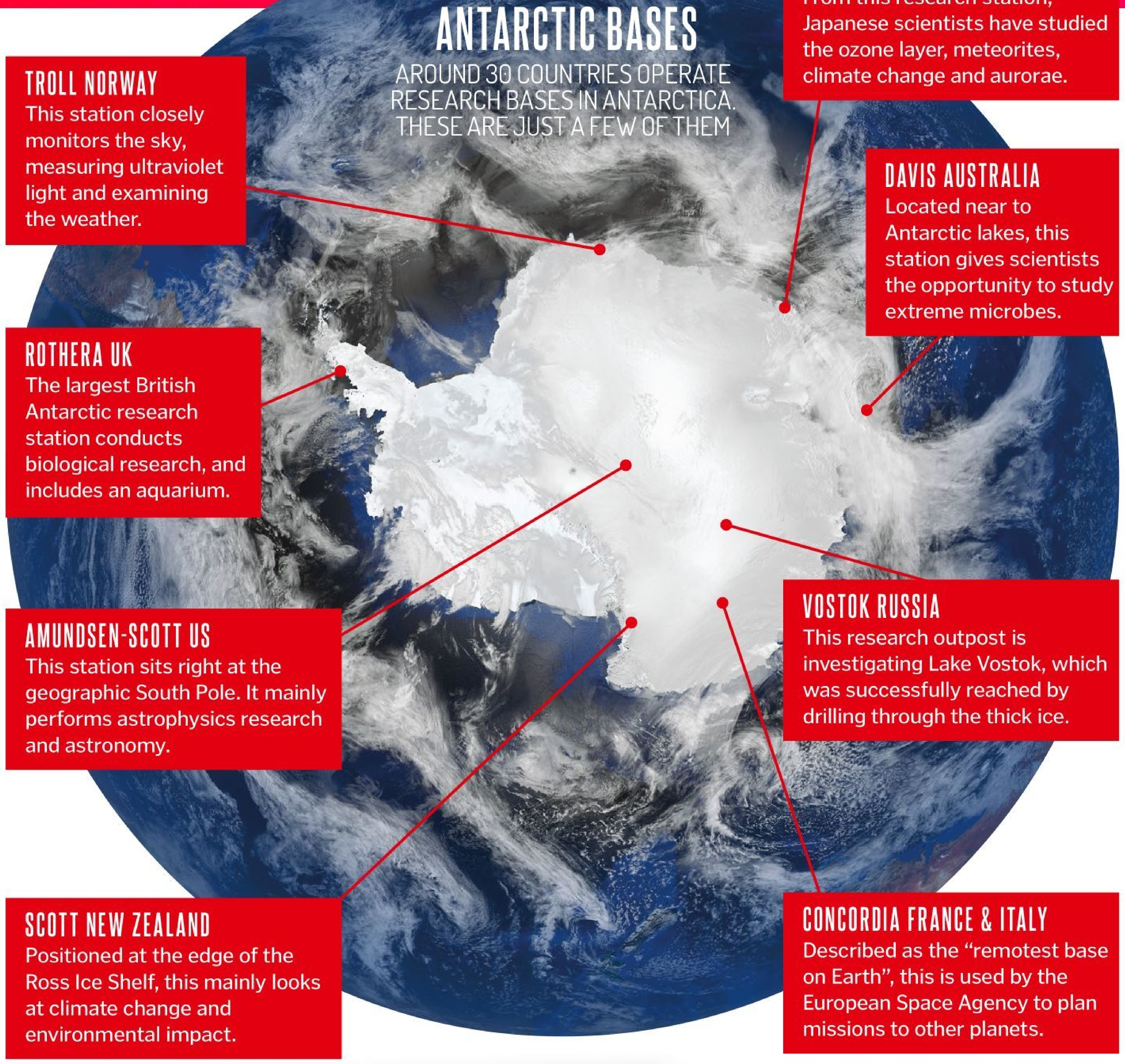
The weather in the Antarctic is unforgiving. Fog can descend over the ice, creating a whiteout and making it near impossible to make out the difference between snow and sky. Under these conditions, the crags, cliffs and sheer drops in the ice become invisible.

In the field, research teams shelter in tents and huts specially designed to resist the weather. Airbeds and sheepskins keep them as far from the frozen ground as possible, and insulated down-filled sleeping bags keep them warm. Layers of woollen clothes, topped off with wind and waterproof outerwear are also used.

Each scientist has a ration box that provides 3,500 calories per day, and human waste often has to be brought back to base when they're done to protect the environment – that's right, even the nasty stuff. Antarctic research is tough.

ANTARCTIC BASES

AROUND 30 COUNTRIES OPERATE RESEARCH BASES IN ANTARCTICA. THESE ARE JUST A FEW OF THEM



TROLL NORWAY
This station closely monitors the sky, measuring ultraviolet light and examining the weather.

ROTHERA UK
The largest British Antarctic research station conducts biological research, and includes an aquarium.

AMUNDSEN-SCOTT US
This station sits right at the geographic South Pole. It mainly performs astrophysics research and astronomy.

SCOTT NEW ZEALAND
Positioned at the edge of the Ross Ice Shelf, this mainly looks at climate change and environmental impact.

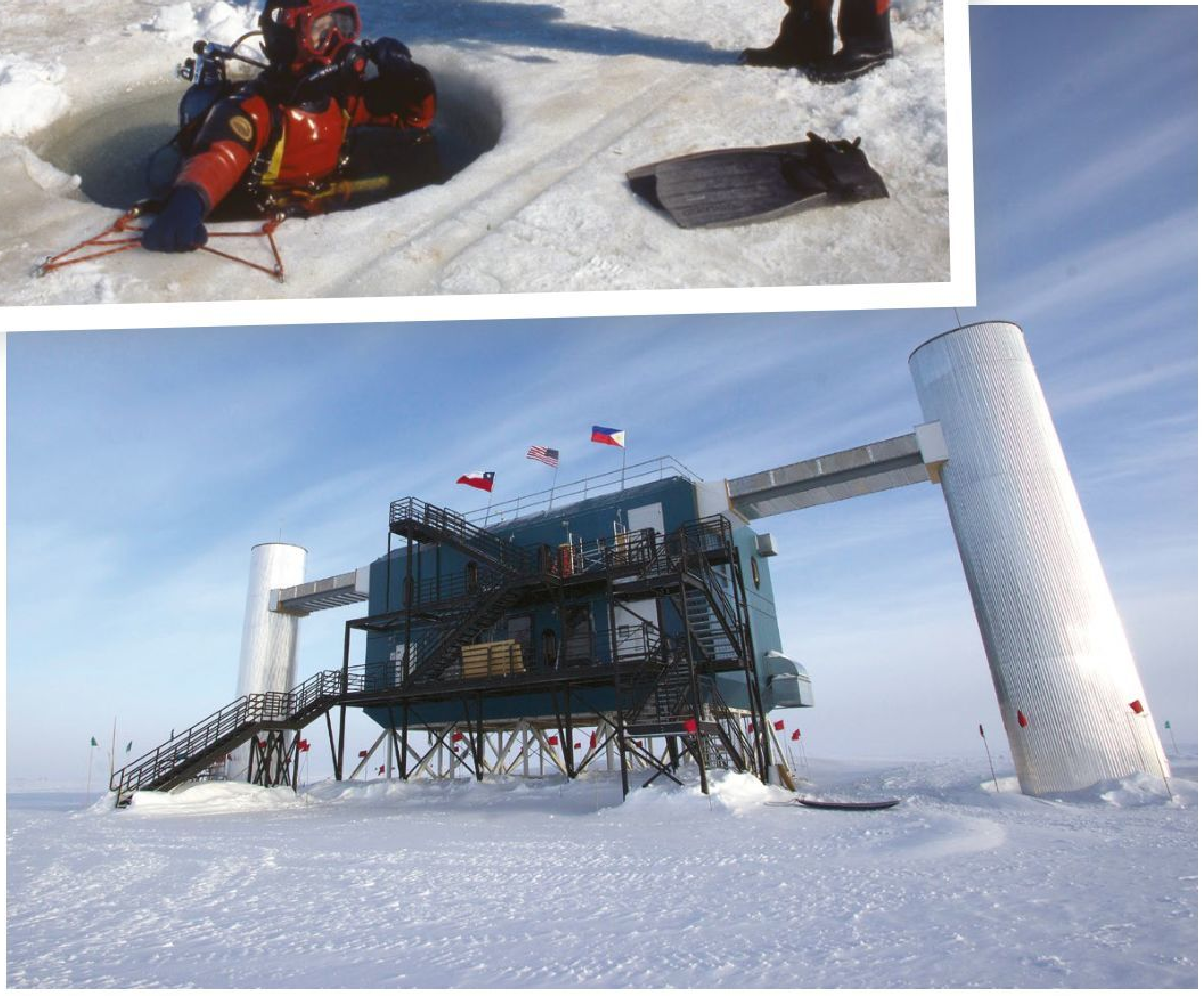
SYOWA JAPAN
From this research station, Japanese scientists have studied the ozone layer, meteorites, climate change and aurorae.

DAVIS AUSTRALIA
Located near to Antarctic lakes, this station gives scientists the opportunity to study extreme microbes.

VOSTOK RUSSIA
This research outpost is investigating Lake Vostok, which was successfully reached by drilling through the thick ice.

CONCORDIA FRANCE & ITALY
Described as the "remotest base on Earth", this is used by the European Space Agency to plan missions to other planets.

A diver dressed in thermal protective gear takes an icy plunge for underwater-based research



The IceCube Neutrino Observatory is buried deep beneath the ice

WHY THEY DO IT

TO STUDY A UNIQUE ENVIRONMENT
Antarctica is wild and inhospitable to life.

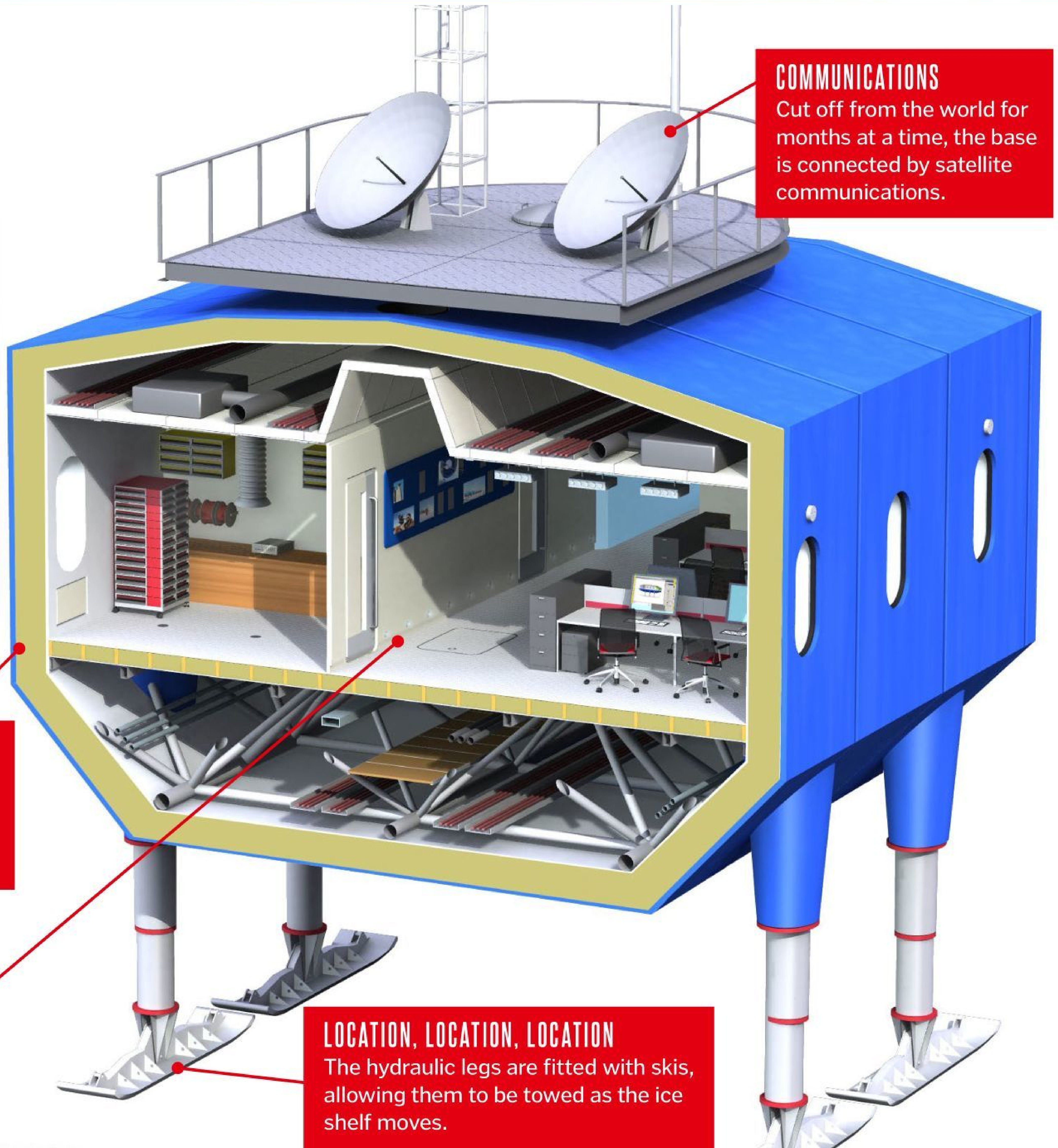
TO MONITOR CLIMATE CHANGE
The ice is vulnerable to changes in temperature.

TO OPEN A TIME CAPSULE
Locked away in the ice is information about Earth's history.

The British Antarctic Survey's Halley VI base is built on skis

HALLEY VI BASE

THIS BRITISH RESEARCH STATION IS PERCHED ON AN ICE SHELF THAT MOVES HALF A METRE INTO THE SEA EVERY DAY

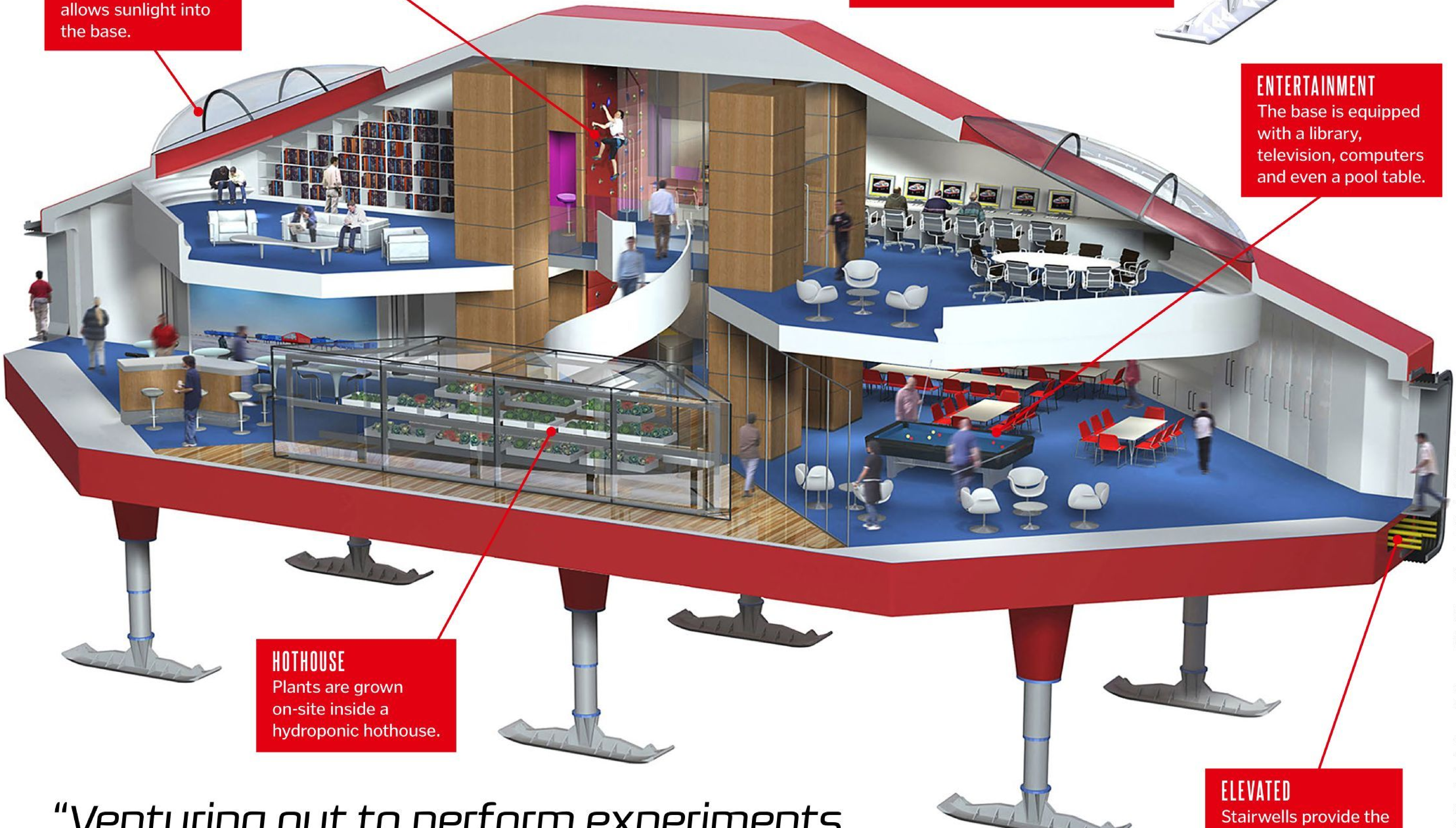


COMMUNICATIONS
Cut off from the world for months at a time, the base is connected by satellite communications.

MODULES
The modules are strung together in a chain, with bedrooms on one side and labs on the other.

CLIMATE MONITORING
Halley is a crucial base for monitoring long-term weather and climate trends.

LOCATION, LOCATION, LOCATION
The hydraulic legs are fitted with skis, allowing them to be towed as the ice shelf moves.



KEEPING ACTIVE
The base even has its own climbing wall, which helps the staff to exercise inside.

NATURAL LIGHT
A strong glass ceiling allows sunlight into the base.

ENTERTAINMENT
The base is equipped with a library, television, computers and even a pool table.

HOTHOUSE
Plants are grown on-site inside a hydroponic hothouse.

ELEVATED
Stairwells provide the only means of getting in or out of the base.

> "Venturing out to perform experiments poses the biggest danger"

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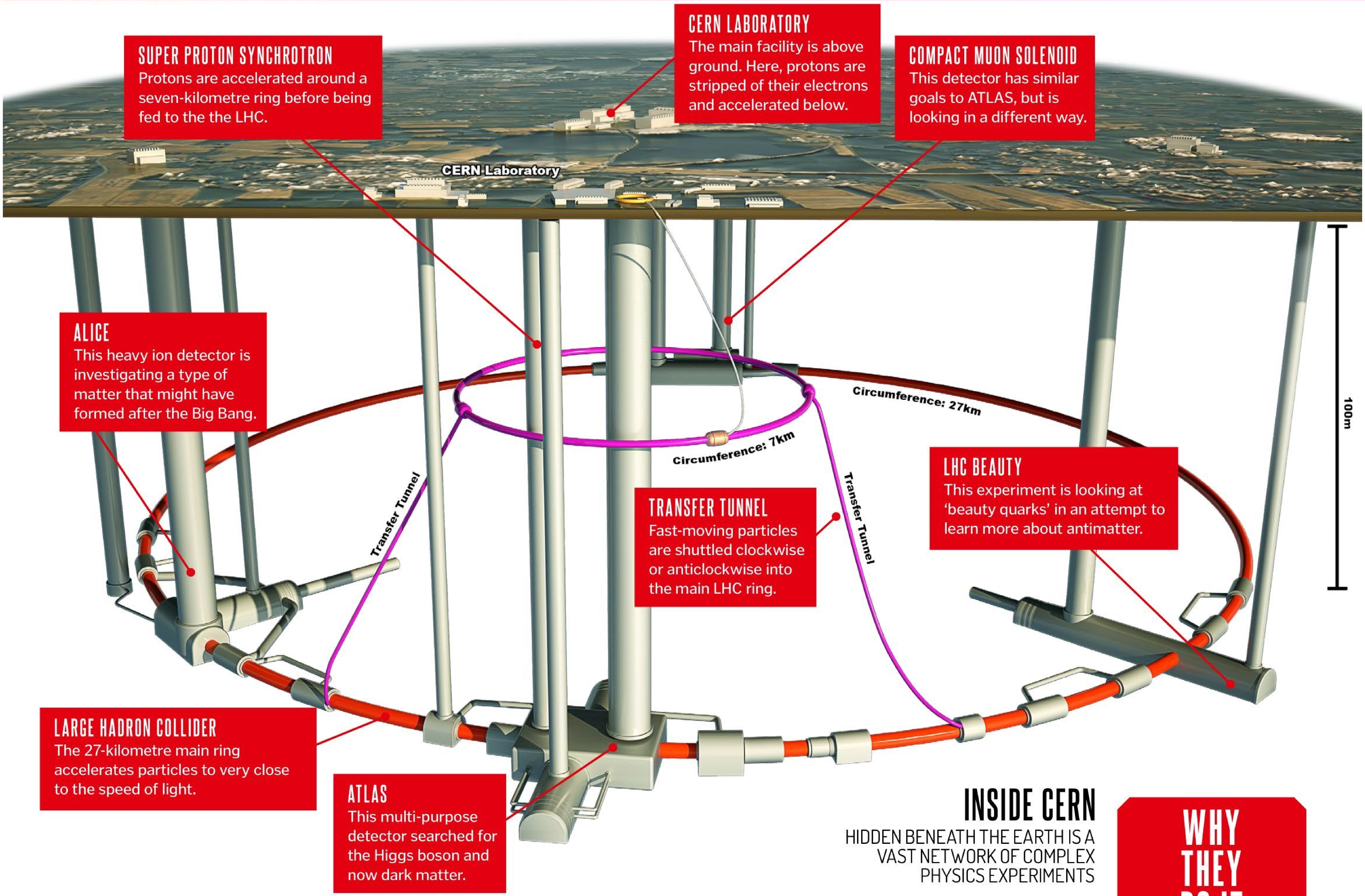


SUPER PROTON SYNCHROTRON
Protons are accelerated around a seven-kilometre ring before being fed to the the LHC.

CERN LABORATORY
The main facility is above ground. Here, protons are stripped of their electrons and accelerated below.

COMPACT MUON SOLENOID
This detector has similar goals to ATLAS, but is looking in a different way.

ALICE
This heavy ion detector is investigating a type of matter that might have formed after the Big Bang.

LHC BEAUTY
This experiment is looking at 'beauty quarks' in an attempt to learn more about antimatter.

TRANSFER TUNNEL
Fast-moving particles are shuttled clockwise or anticlockwise into the main LHC ring.

LARGE HADRON COLLIDER
The 27-kilometre main ring accelerates particles to very close to the speed of light.

ATLAS
This multi-purpose detector searched for the Higgs boson and now dark matter.

INSIDE CERN

HIDDEN BENEATH THE EARTH IS A VAST NETWORK OF COMPLEX PHYSICS EXPERIMENTS

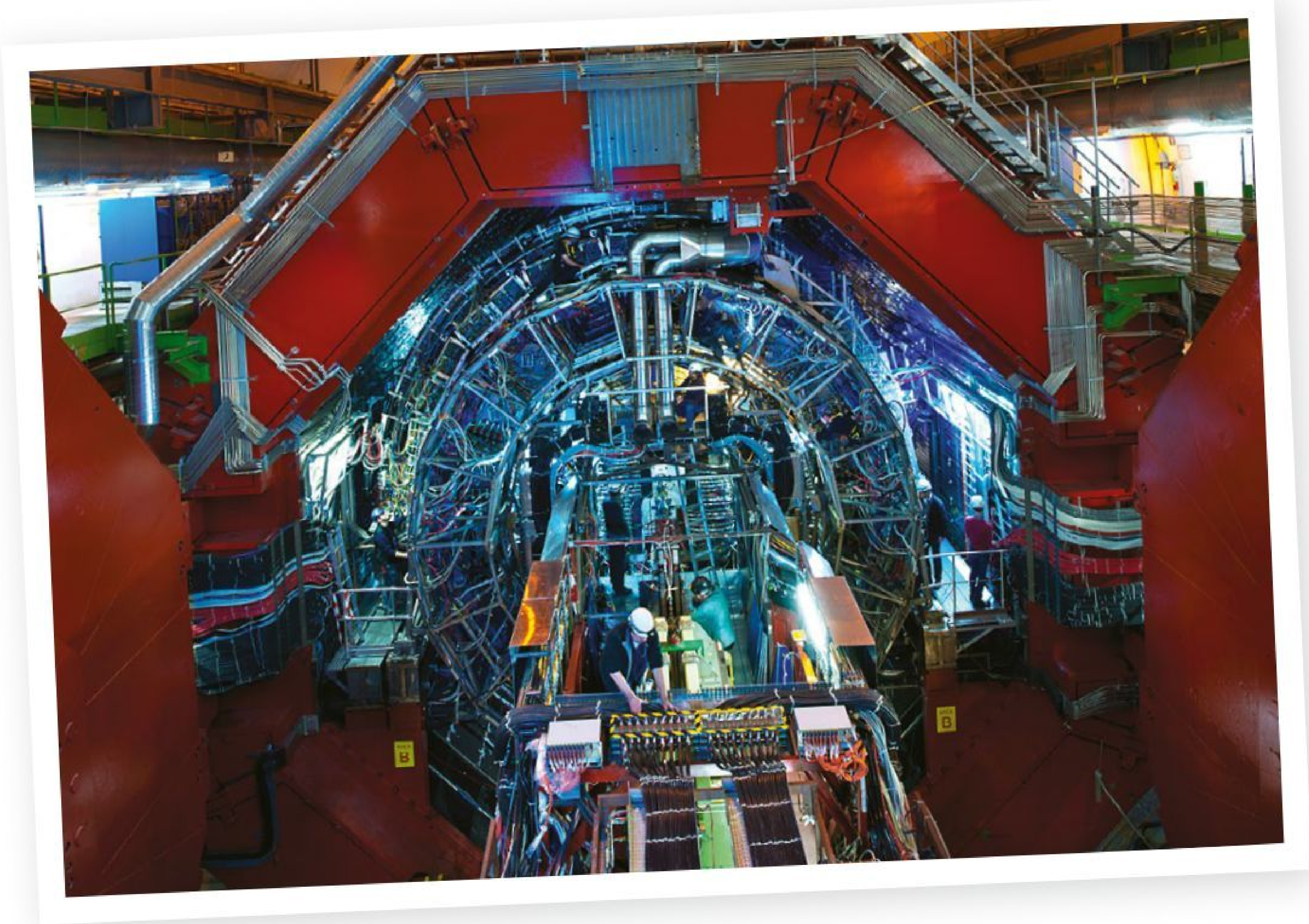
EXTREME PHYSICS

CERN IS THE WORLD'S LARGEST, AND MOST FAMOUS, PHYSICS LAB

This underground physics lab is one of the most cutting-edge facilities anywhere on the planet. It is located across the border of France and Switzerland, and is jointly operated by 22 member states, together known as the 'European Council for Nuclear Research' (CERN). The facility is home to the world's largest scientific instrument, the famous Large Hadron Collider (LHC), which is used to explore the fundamental structure of the universe.

The LHC is a ring-shaped particle accelerator, measuring a staggering 27 kilometres around its circumference. Particles are fed into this ring, and over 1,500 superconducting magnets guide them around this underground racecourse at almost the speed of light, until they violently slam together.

CERN assures us that there is no danger of creating a world-ending black hole; the main purpose of these experiments is to search for answers. The CERN team want to find out why there is more matter than antimatter in the universe – they should, theoretically, be equal. They are also still experimenting with the Higgs boson – a particle that is important for explaining why other particles have mass, following its discovery. And they want to learn more about dark matter and dark energy.



ATLAS is one of CERN's most famous detectors – its task is to search for dark matter

WHY THEY DO IT

TO UNDERSTAND THE UNIVERSE
Particle physics underpins every other science.

TO EXPLORE ANTIMATTER
To find out why our universe is mostly made of matter.

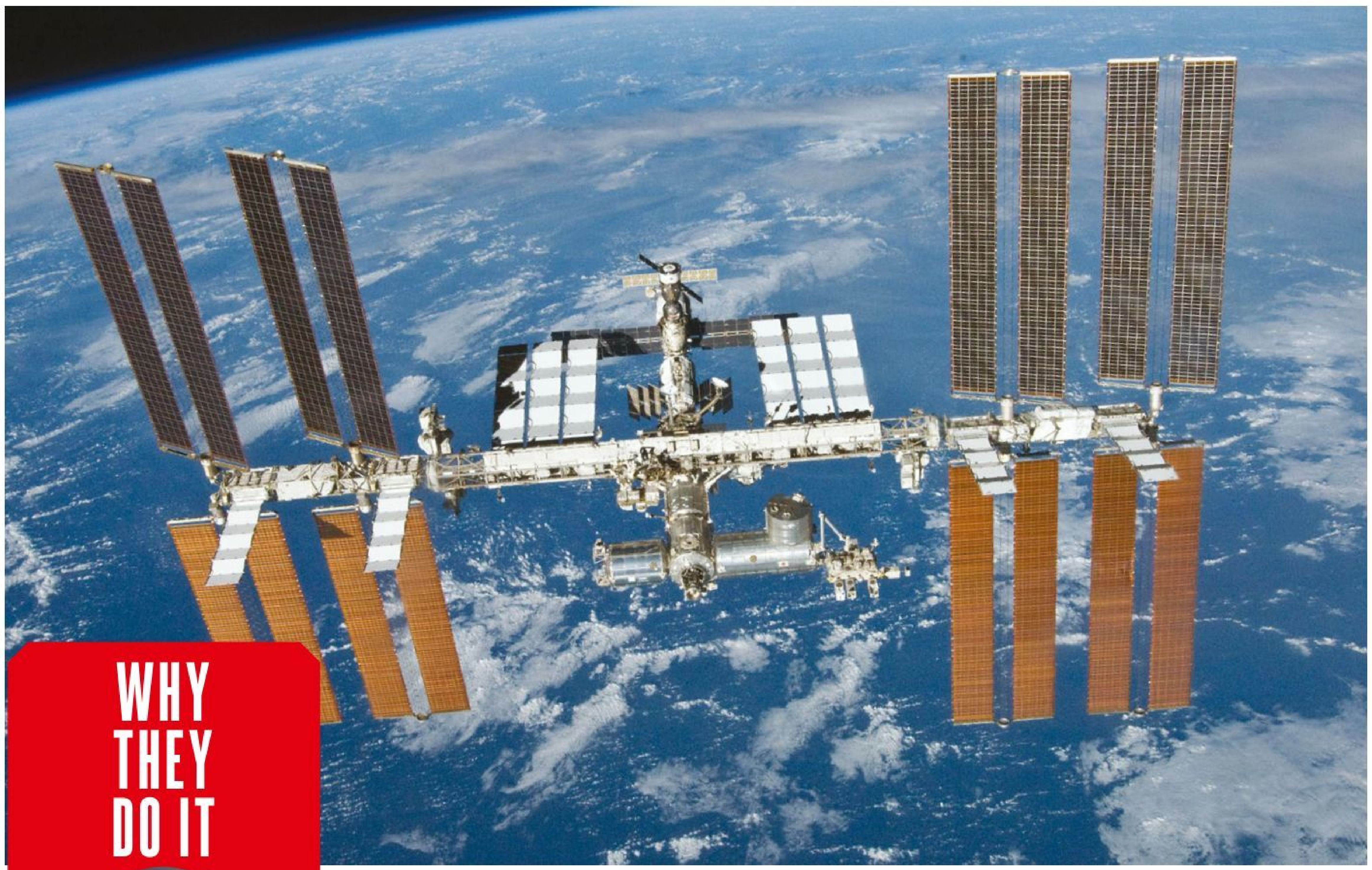
TO WORK ON THE HIGGS BOSON
This particle helps to explains why other particles have mass.

SCIENCE IN SPACE

THE ISS IS ONE OF THE MOST IMPRESSIVE LABORATORIES EVER BUILT

The International Space Station is one of the greatest feats of human endeavour. This orbital laboratory circles the Earth at a height of 400 kilometres, with a permanent crew of at least three astronauts. Away from the fierce tug of Earth's gravity, the crew and equipment onboard are weightless, and in this strange environment all kinds of different experiments can be performed.

Microgravity affects the way that living organisms tell up from down, and it changes the way that chemicals behave. Experiments on cells, small animals, and the astronauts themselves, are helping scientists to understand the impact space has on life. It's the perfect place to test new ideas and technology for future space missions, and it is also a great spot to monitor what's happening back on the Earth below.



WHY THEY DO IT

TO UNDERSTAND OUTER SPACE
This unique environment allows constant access to microgravity.

TO MONITOR THE EARTH
They can watch how the Earth changes over time.

FOR THE FUTURE
The ISS is a test area for future long-term space missions.

○ Astronaut, Kate Rubins, was the first person ever to sequence DNA in space

○ Microgravity has strange effects on fire; this equipment allows astronauts to study it

○ Human cells can be grown on the space station for experiments, like these stem cells

SERIOUSLY SCARY SCIENCE

FROM TWISTERS TO DISEASES, THESE SCIENTISTS ARE ON THE FRONT LINES

CHASING STORMS

These extreme-weather scientists run towards dangerous storms in specially-adapted vehicles. Carrying cameras, communications equipment, Doppler radars and weather balloons, they get up close and personal with tornadoes.

DEADLY PREDATOR STUDIES

Physiologists and conservationists work with some of the most dangerous animals on the planet, bringing crocodiles, lions, bears and elephants down to be tagged, tracked and sampled.

INFECTIOUS DISEASE SCIENTISTS

Preventing, controlling and curing deadly infections takes years of research. Scientists working on diseases like Ebola need to get close to samples in their labs, but not without layers of strict protection.

FREAKY PHENOMENA

DON'T BE ALARMED – SCIENCE SHOWS THAT THE PARANORMAL IS NORMAL AFTER ALL

We are masters of pattern recognition, taking in vast quantities of data and searching for the links that make sense of the world around us. As humans, we are always seeking to explain the unexplained, and there's nothing we find more disturbing than not being able to find an answer.

For centuries, the paranormal explained the unexplained, but now science is stepping in. Think you may have seen a ghost? You're probably over tired. Sure you've heard voices in a backwards music track? It's more likely to be your brain desperately looking for patterns. Extraordinary occurrences almost always have a mundane explanation.

○ The light at the end of the tunnel is just loss of blood flow to the back of the eye

SEEING FACES

Have you ever woken up in the middle of the night to find a figure looming over your bed, only to realise that it's actually a pile of clothes? Or perhaps you've seen a spooky face peering through your window only to have it disappear when the wind ruffles the leaves. You might have experienced pareidolia. The word literally means 'wrong image', and it's down to the way our brains hunt for patterns.

We process a constant stream of sensory information, and our brains have fractions of seconds to make decisions. This means storing and recalling simple patterns so that we can quickly scan through the noise. In much the same way as your smartphone camera looks for patterns to draw boxes around faces, your brain hones in on anything that might have two eyes and a mouth.

○ Our facial-recognition system looks for two eyes and a mouth

○ The brain stops sending signals to the muscles when we dream

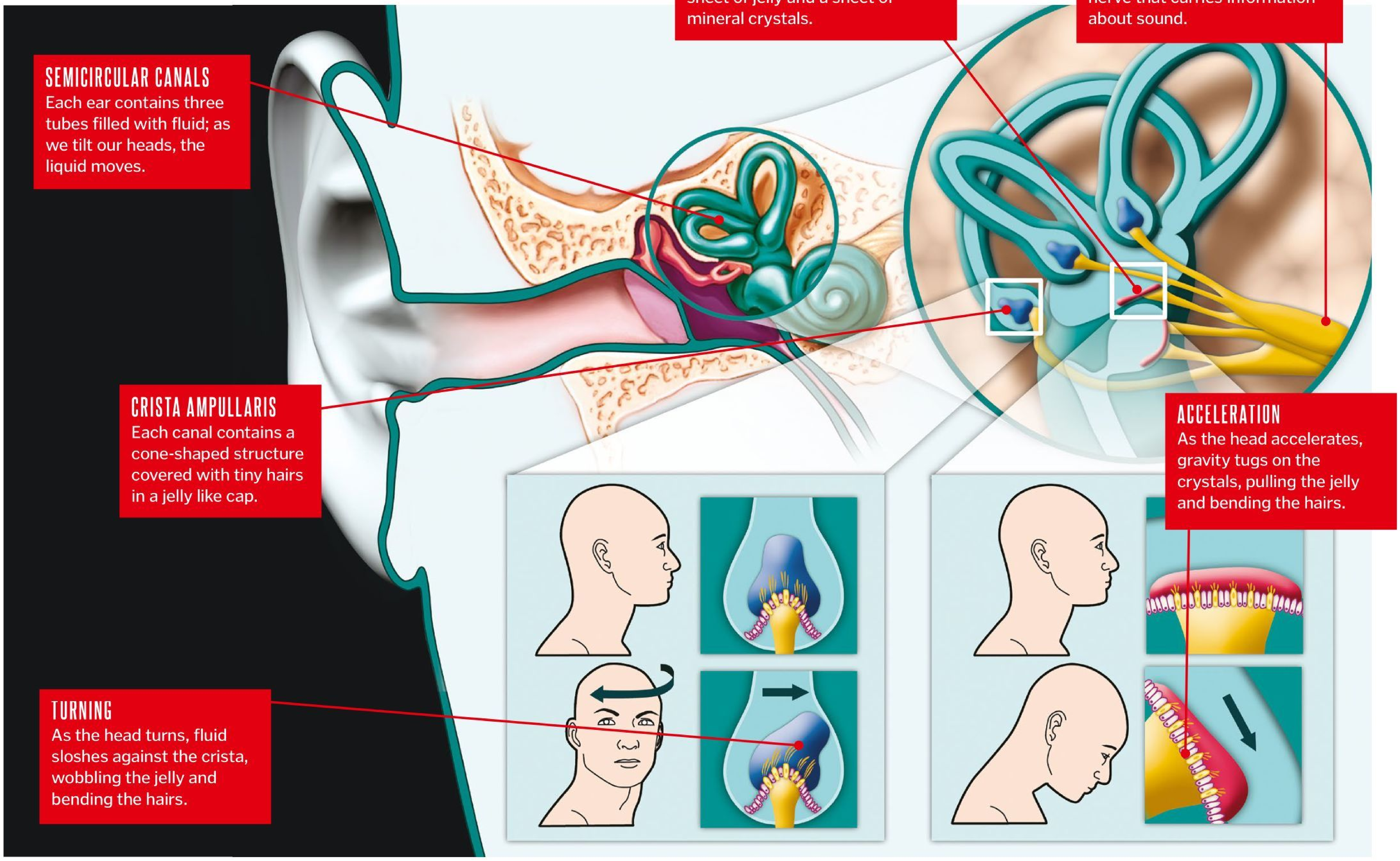
SLEEP PARALYSIS

Waking to the awful feeling that you've lost control of your limbs can be terrifying, but sleep paralysis is essential to keep you safe at night. When we dream during rapid eye movement (REM) sleep, our brains run through vivid simulations and try to send messages to our muscles. But two signalling chemicals, gamma-aminobutyric acid (GABA) and glycine, stop messages reaching the motor neurons. This prevents us from acting out our dreams and harming ourselves and others, but sometimes the system can experience a malfunction.

The frightening experience of sleep paralysis happens when our brains enter this dream-like state when we're still awake. It's rare but occurs more often if we're over tired, have jet lag or work irregular shifts that mess with our body clocks.

THE BODY'S SPIRIT LEVEL

TWISTED TUBES OF FLUID IN THE EARS TELL THE BRAIN WHICH WAY IS UP



MACULA OF UTRICLE
Under the canals are flat pouches containing a sheet of hairs, a sheet of jelly and a sheet of mineral crystals.

VESTIBULOCOCHLEAR NERVE
Information about balance travels to the brain via the same nerve that carries information about sound.

SEMICIRCULAR CANALS
Each ear contains three tubes filled with fluid; as we tilt our heads, the liquid moves.

CRISTA AMPULLARIS
Each canal contains a cone-shaped structure covered with tiny hairs in a jelly like cap.

ACCELERATION
As the head accelerates, gravity tugs on the crystals, pulling the jelly and bending the hairs.

TURNING
As the head turns, fluid sloshes against the crista, wobbling the jelly and bending the hairs.

THE SCIENCE BEHIND NEAR-DEATH EXPERIENCES

1 FEELING LIKE YOU'RE DEAD

In rare situations, problems with the brain can make the living feel as though they are dead. Known as Cotard's delusion, or 'walking corpse syndrome', this rare mental illness can occur when certain neurological disorders interfere with signals in the brain.

2 MOVING TOWARDS THE LIGHT

The infamous light at the end of the tunnel might simply be down to a loss of blood flow triggered by fear or disease. When the back of the eye can't get enough oxygen, the edges of your vision can start to fade.

3 SEEING DEAD PEOPLE

Hallucinations can make us believe that we can see or hear long lost loved ones, but they are just a trick of the brain. They can occur for many reasons, ranging from brain damage and mental illness to just being tired.

4 FEELINGS OF EUPHORIA

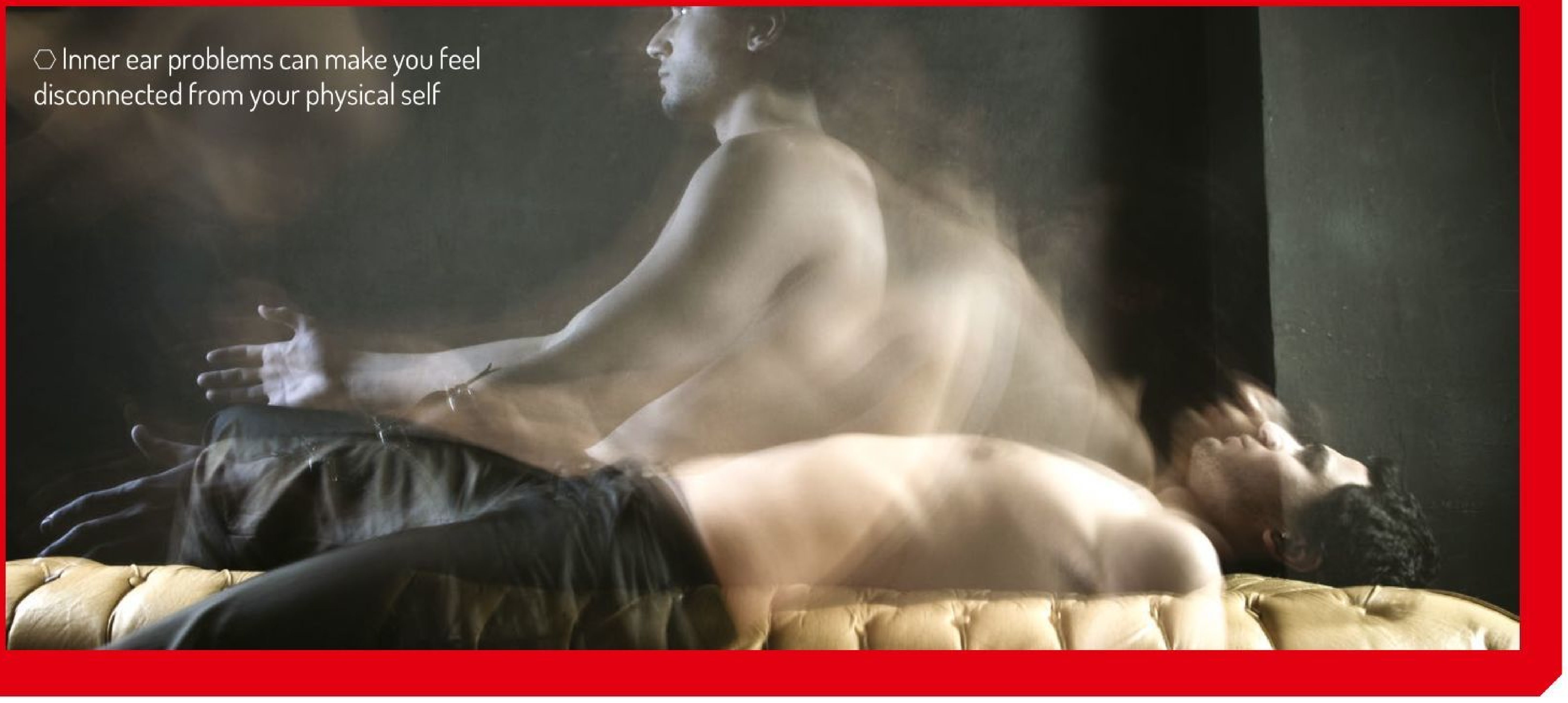
Fear triggers the body's fight-or-flight response, making the brain produce powerful chemicals that change the way we think and feel. These include adrenaline and dopamine, which kill pain and can induce intense feelings of elation and euphoria.

OUT-OF-BODY EXPERIENCES

Few experiences could be weirder than finding yourself looking down at your own body from above. However, there may be a solid scientific explanation. People with certain neurological disorders are more likely to have an out-of-body experience, so studying their brains can reveal clues about why they happen.

In 2002, while undergoing an evaluation for epilepsy, a patient allowed scientists to insert electrical signals into their brain. Some of these signals triggered an out-of-body experience. The part of the brain responsible was the right angular gyrus, which links information from the eyes and the inner ear. The inner ear contains a set of fluid-filled tubes that work as the body's spirit level. Problems here can literally throw you off balance, triggering a spell of dizziness, floating feelings and disorientation.

A larger study in 2017 found that people with inner ear problems were almost three times as likely to have had an out-of-body experience. It seems that a mismatch between what you see and what you feel can trick your brain into thinking that you've left your body behind.



○ Inner ear problems can make you feel disconnected from your physical self

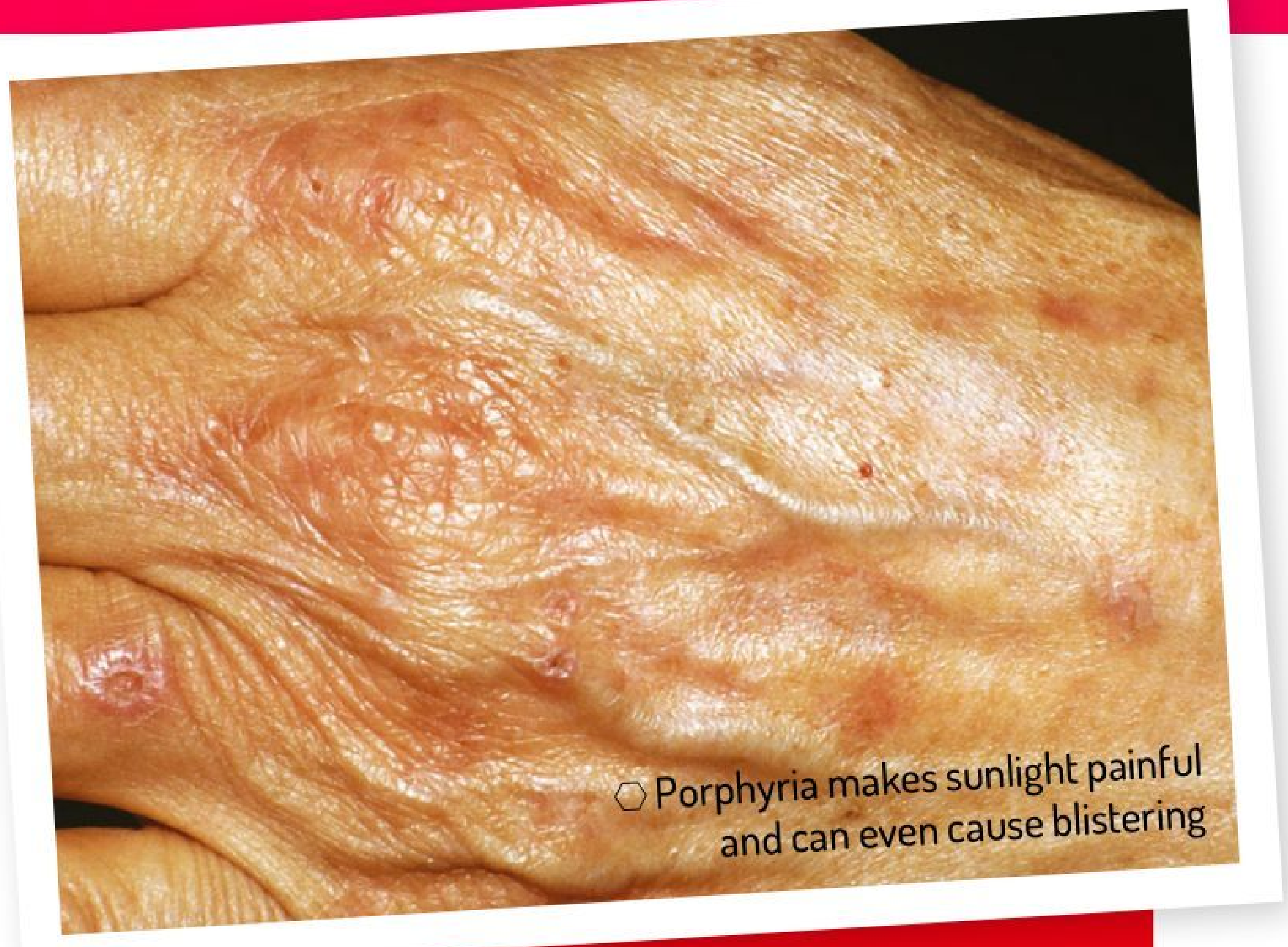
© Getty

DEBUNKING THE VAMPIRE MYTH

HOW SCIENCE CAN EXPLAIN THE PHENOMENA THAT LED MANY PEOPLE TO BELIEVE IN THE UNDEAD

Legends of beings that defied death and preyed on the living date back to ancient times. Many early civilisations featured vampiric creatures in their lore, such as the terrifying child-eating demon Lamia of ancient Greek mythology and the life-sucking edimmu ghosts of Mesopotamian legend.

The belief in vampires became particularly common in the folklore of medieval Europe and persisted for hundreds of years, the superstitions often resurfacing during outbreaks of plague and other illnesses. But as our scientific understanding improved, the mysteries at the root of these beliefs were unravelled. Large fangs, hypersensitivity to sunlight and blood around the mouth could all be explained by then-unknown diseases and the natural process of decay after death.



○ Porphyria makes sunlight painful and can even cause blistering

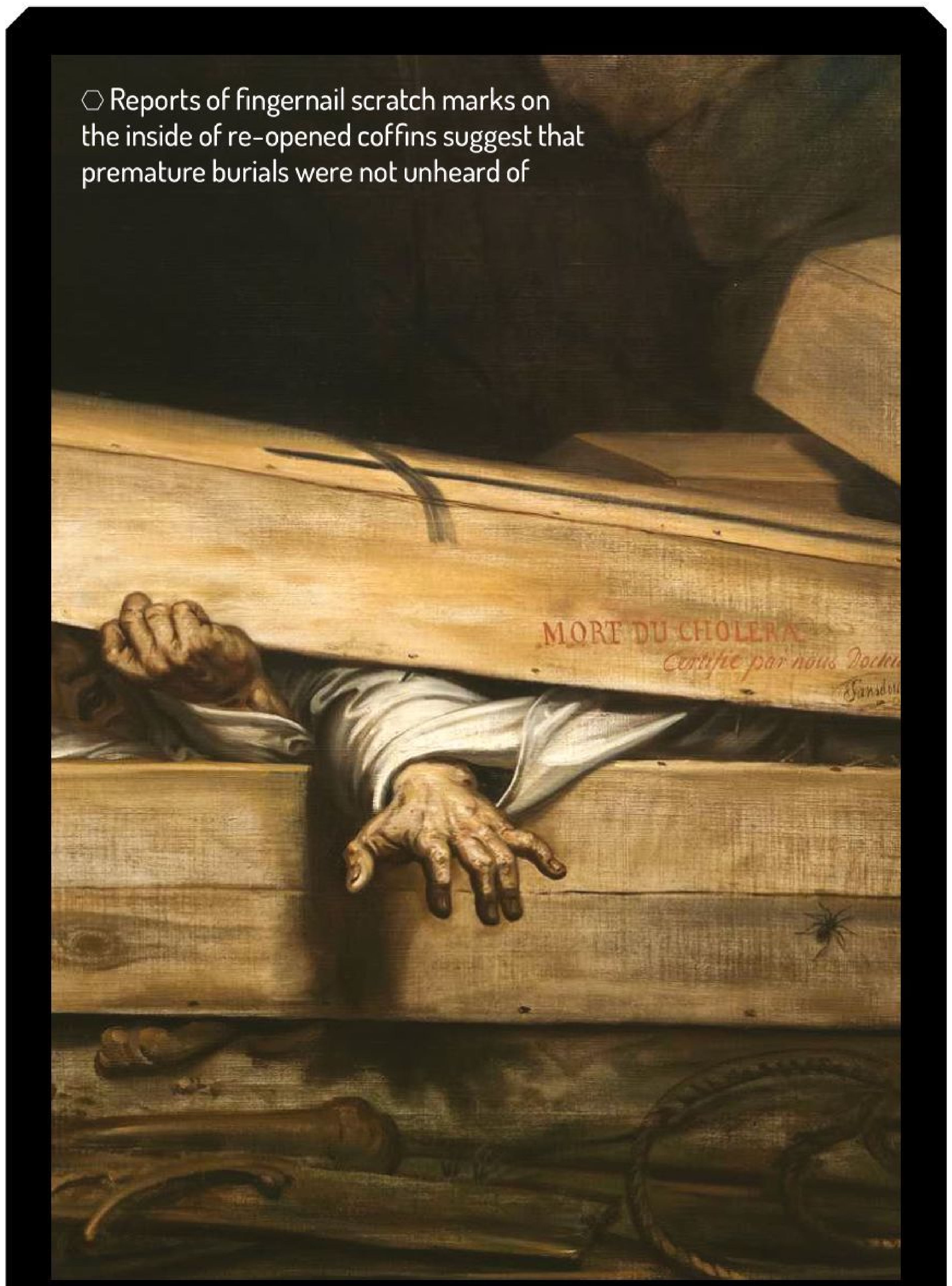
FANGS, SUNLIGHT AND GARLIC

The classic vampires of legend have prominent fangs to pierce their victims' necks, are nocturnal and have pale skin due to their aversion to sunlight. They can also be warded off with garlic. Thanks to medical advances, these days we know of several conditions that could actually explain some of these features.

Porphyria is a group of conditions that may have contributed to the vampire myth. One type, called congenital erythropoietic porphyria (CEP), causes a toxic build-up of light-activated molecules in the skin. When sufferers are exposed to sunlight these toxins can eat away at the skin, damaging the gum tissue to make teeth look longer and fang-like. As well as Sun sensitivity, porphyria can also make people hypersensitive to foods high in sulphur, such as garlic.

Similar symptoms can be experienced by those suffering from rabies, a deadly virus that can be transmitted to humans if bitten by an infected animal. Rabid people can develop insomnia, become aggressive – even trying to bite people – and demonstrate an aversion to strong stimuli, including bright light and strong smells like garlic. The diagnosis of rabies also fits the common depiction of male vampires pursuing female victims. The condition is seven times more common in men and can cause an increased libido by affecting the body's limbic system.

○ The rabies virus is transmitted to humans via animal bites, often from infected dogs



Reports of fingernail scratch marks on the inside of re-opened coffins suggest that premature burials were not unheard of

BURIED ALIVE

Fear of the dead rising again meant that the living would sometimes take some rather macabre precautions to ensure this didn't happen. Positioning a sickle around the body's neck in the coffin, stabbing the corpse through the chest or slicing its knee tendons were just some of the methods used during burials to make sure the dead couldn't escape.

The belief that the dead might not stay that way was likely influenced by horrifying cases of people being buried alive. Poor medical knowledge meant that victims could be mistakenly declared dead and buried prematurely, only to regain consciousness when it was too late. For example, people with catalepsy can have seizures in which the body goes stiff and the breathing and heart rate slows dramatically, which could easily lead to a false diagnosis of death.

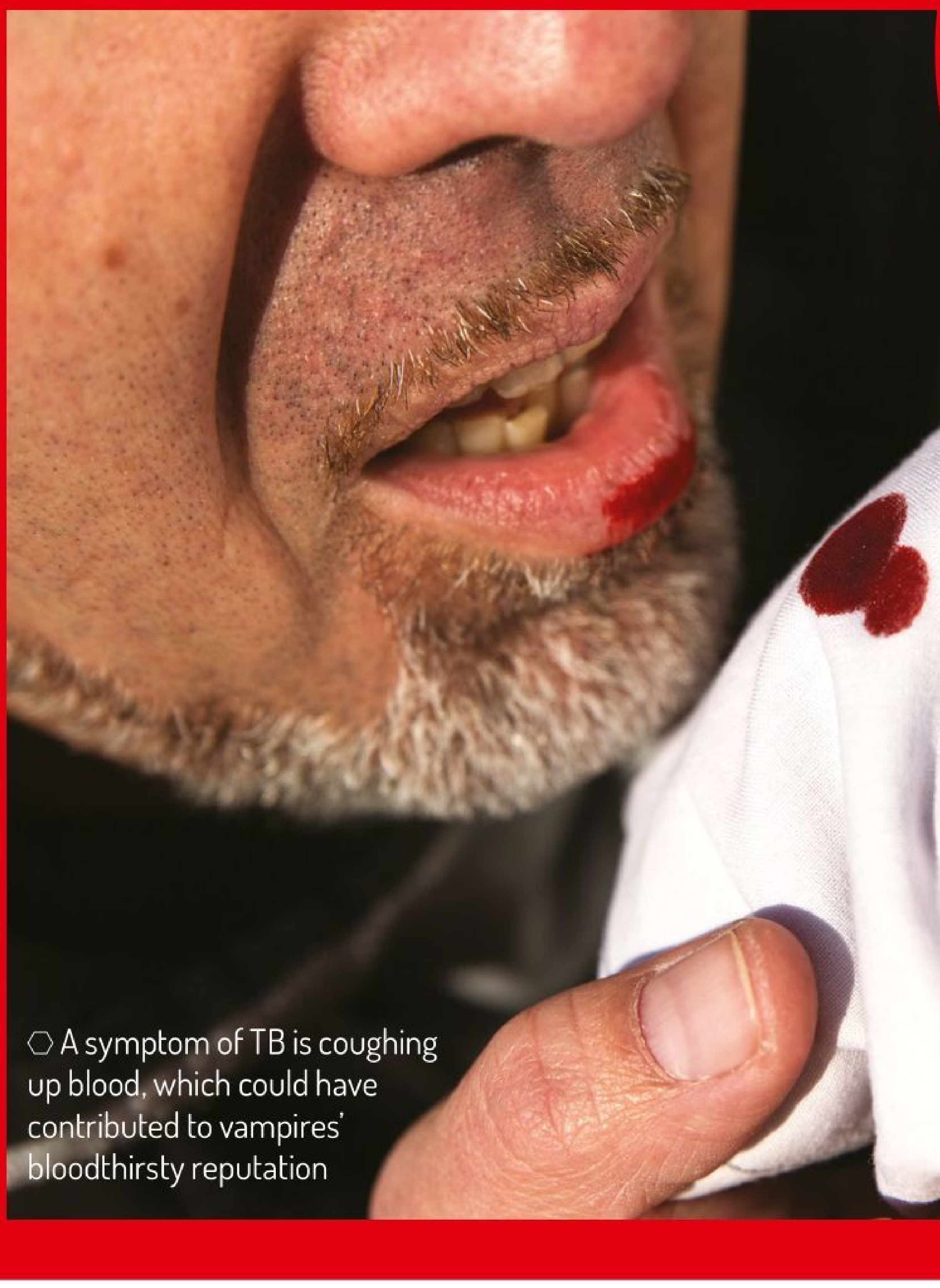
A THIRST FOR BLOOD

In times when people were wary of vampires, corpses were occasionally dug up to check they were still dead. People's fears were exacerbated when bodies were found to have blood oozing from the nose and mouth. In reality, what looked like blood was actually 'purge fluid', the result of the natural decay process as the internal organs start to break down.

Symptoms of disease also contributed to the blood-sucking myth. Tuberculosis (TB) is a bacterial infection that primarily affects the lungs and causes sufferers to cough up blood. Before the illness was understood people blamed these mysterious deaths on supernatural forces. The New England 'vampire panic' in the early 1800s, for example, was a TB outbreak that affected entire families. The deaths were blamed on the first victim of the family somehow feeding off their surviving relatives from beyond the grave.

When they exhumed bodies to try and prevent what they assumed was vampiric activity, their worries were (mistakenly) 'confirmed' by the fact that TB victims would often be found with their mouths full of blood.

German physician Robert Koch won the 1905 Nobel Prize for discovering that TB was caused by the *Mycobacterium tuberculosis* bacteria (pictured)



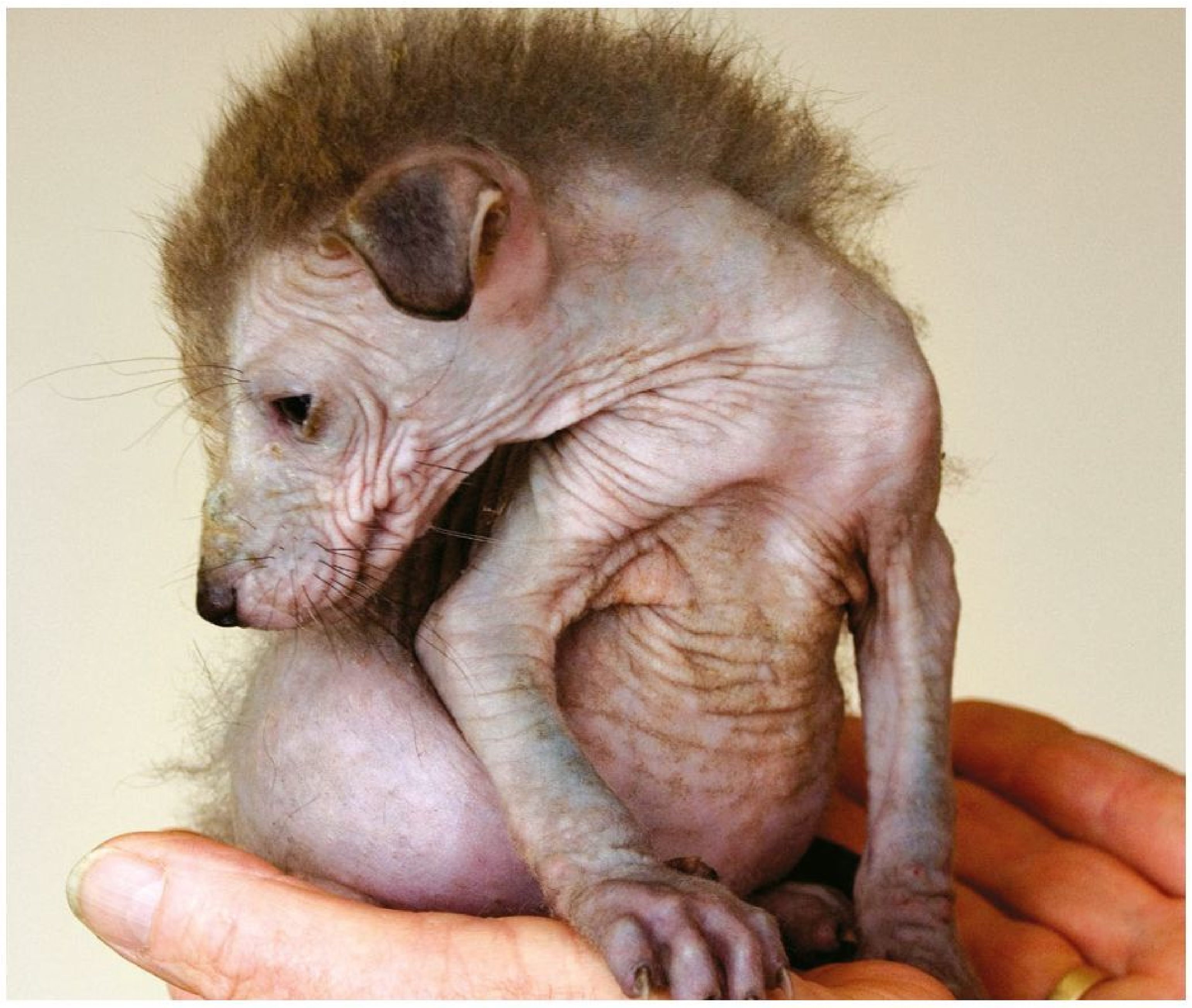
A symptom of TB is coughing up blood, which could have contributed to vampires' bloodthirsty reputation

MANGE AND MOVIE MANIA

In the 1990s, stories of a mysterious creature feeding on the blood of livestock started to emerge in Puerto Rico. Locals called the culprit the chupacabra ('goat eater'), describing it as a beast with long claws and spikes along its spine. Its victims would be found with vampire-like puncture wounds on their necks but no sign of other injuries. The tale of the chupacabra soon spread across Latin America and the southern US, but by the 2000s witnesses' descriptions became far less alien. The creature was said to be hairless and canine.

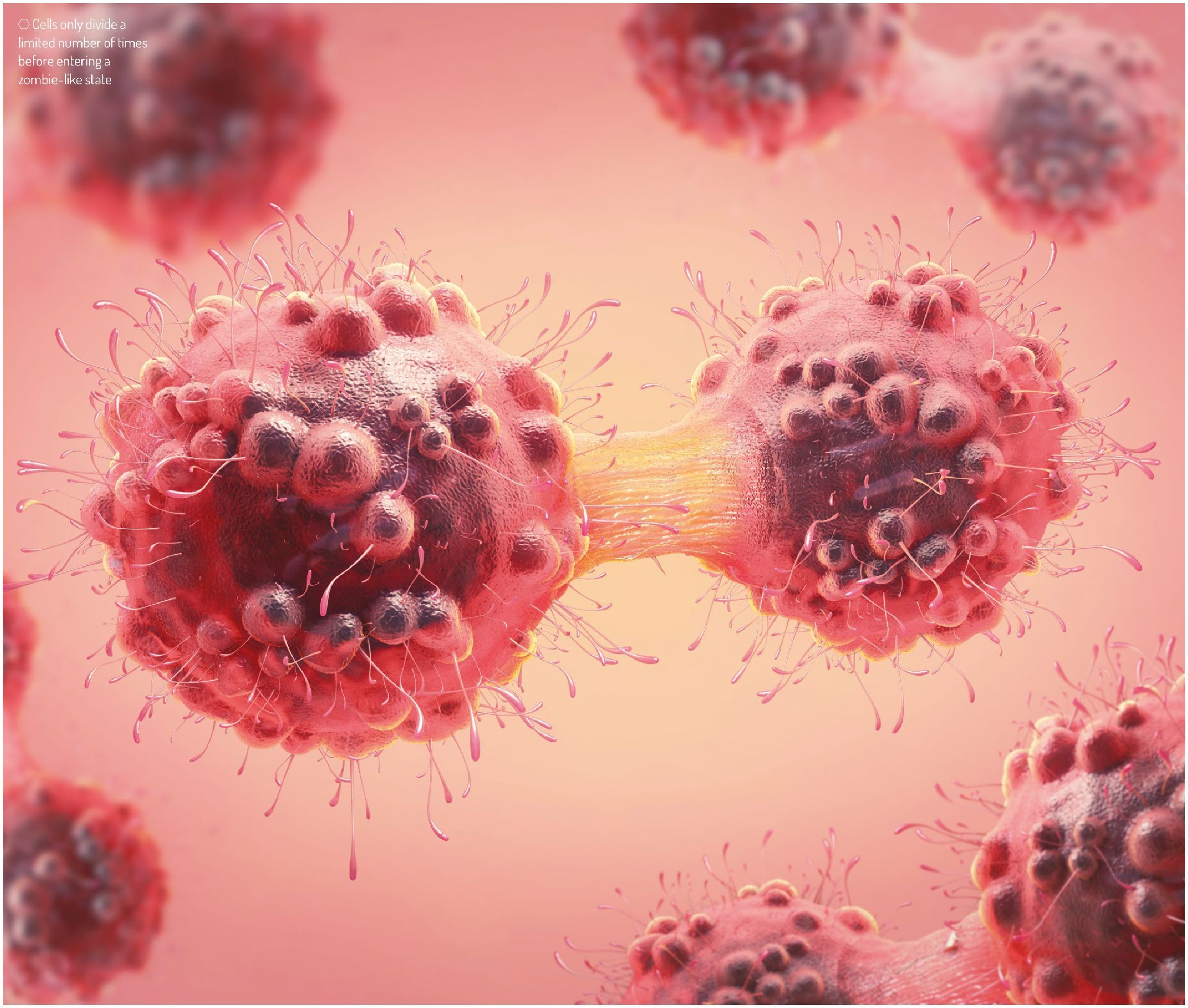
Investigator Benjamin Radford, a research fellow for the Committee for Skeptical Inquiry, set out to find the truth. Over five years he interviewed witnesses and collected evidence, including specimens of livestock victims and alleged chupacabra bodies. DNA analysis of the 'chupacabras' revealed they were coyotes, dogs, or even racoons that suffered from mange, which causes itching, hair loss, inflammation and gauntness. It's also not unusual for dogs and other canines to kill their prey with a bite to the neck and not eat them.

Interestingly, the first sighting of a chupacabra came not long after the alien horror film *Species* was released in Puerto Rico. Radford tracked down the first chupacabra witness and discovered she had watched the film sometime before her sighting, making it likely that the initial reports were in fact just the product of an overactive imagination.



A fox cub with sarcoptic mange, a disease caused by mites that infest the skin. Mange symptoms explain the appearance and behaviour of supposed chupacabras

© Getty; Alamy



⬡ Cells only divide a limited number of times before entering a zombie-like state

UNDEAD CELLS

AS WE AGE, OUR BODIES CLOG UP WITH ZOMBIE CELLS THAT JUST WON'T DIE

Cells have a built-in safety switch that turns them off when they start to get old. They stop dividing, entering a quiet retirement period that scientists call senescence. The old cells send out signals to the immune system, letting it know that they've reached the end of their lives. Then they wait patiently for white blood cells to arrive and shut them down.

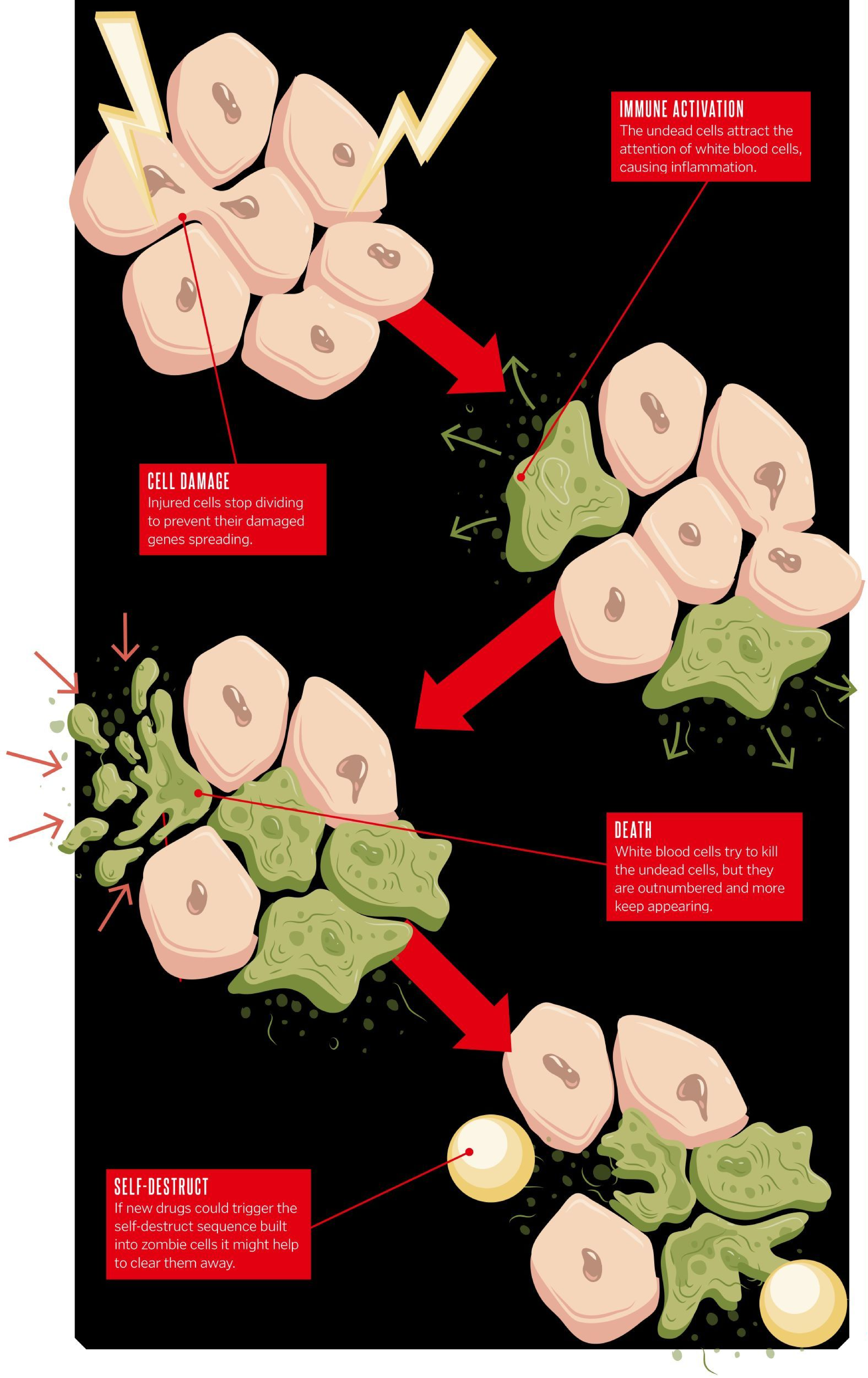
As we get older and more cells enter their twilight years, the immune system can't always keep up with demand. As more and more cells cross over the threshold, the white blood cells get overwhelmed and they stop responding. Undead cells start to build up in tissues, still alive but unable to do their jobs. These zombie cells keep sending out distress signals in the hope that the immune system will come, but all this does is inflame the surrounding tissues. This harms nearby cells, which contributes to the ageing process.

> "These zombie cells keep sending out distress signals"

Scientists found that clearing the undead cells in mice helps to kick-start tissue repair, reversing signs of ageing. Now pharmaceutical companies are racing to find new drugs that can help the immune system to eliminate the undead cells in our own bodies. These zombies have one major weakness – an in-built self-destruct sequence called apoptosis. We just need to find a drug that can push the button and set it off.

ZOMBIE KILLERS

HOW CAN WE GET RID OF THE UNDEAD CELLS CLOGGING UP OUR BODIES?



IMMUNE ACTIVATION
The undead cells attract the attention of white blood cells, causing inflammation.

CELL DAMAGE
Injured cells stop dividing to prevent their damaged genes spreading.

DEATH
White blood cells try to kill the undead cells, but they are outnumbered and more keep appearing.

SELF-DESTRUCT
If new drugs could trigger the self-destruct sequence built into zombie cells it might help to clear them away.

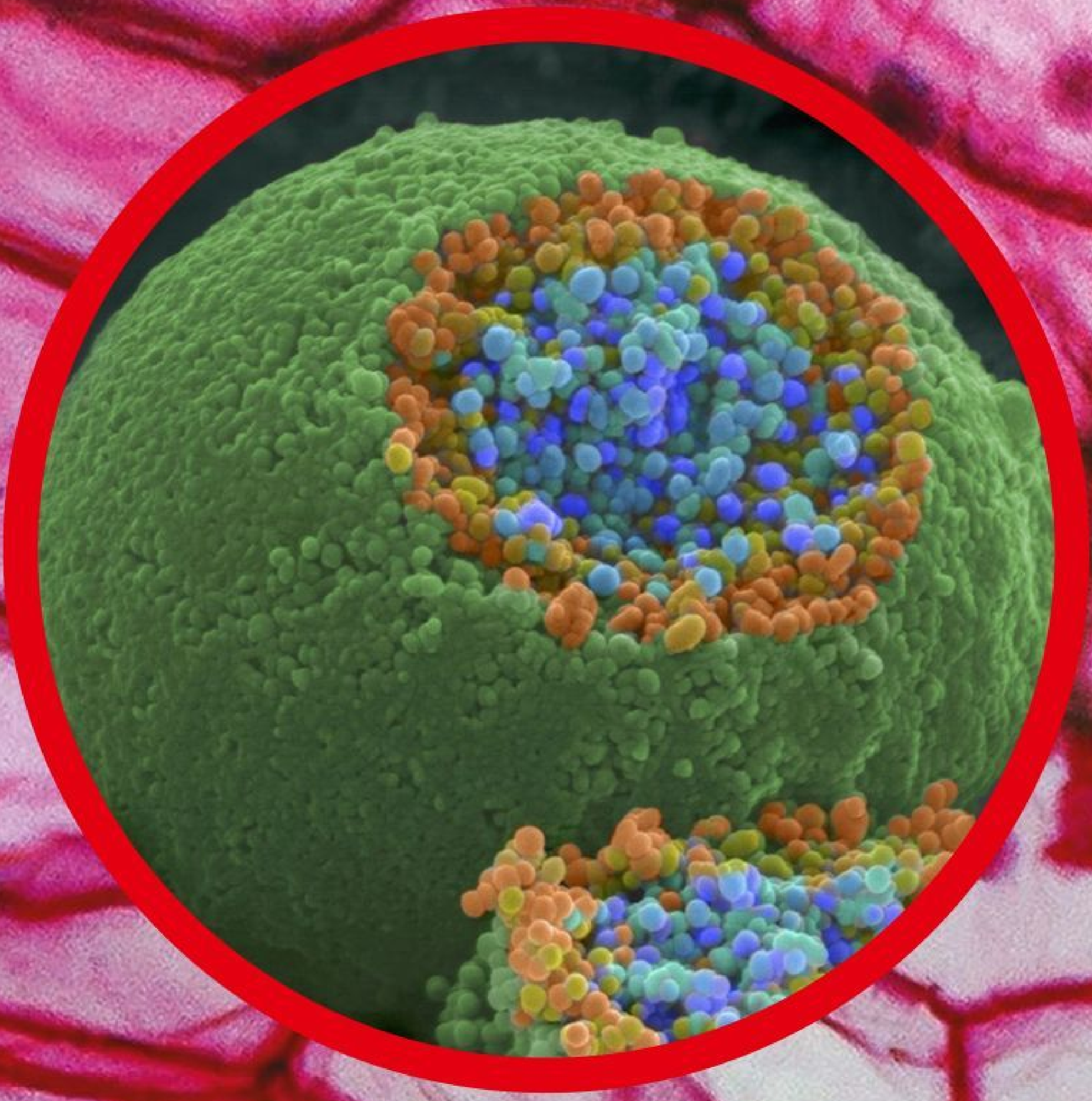
WHAT IS SENESCENCE FOR?

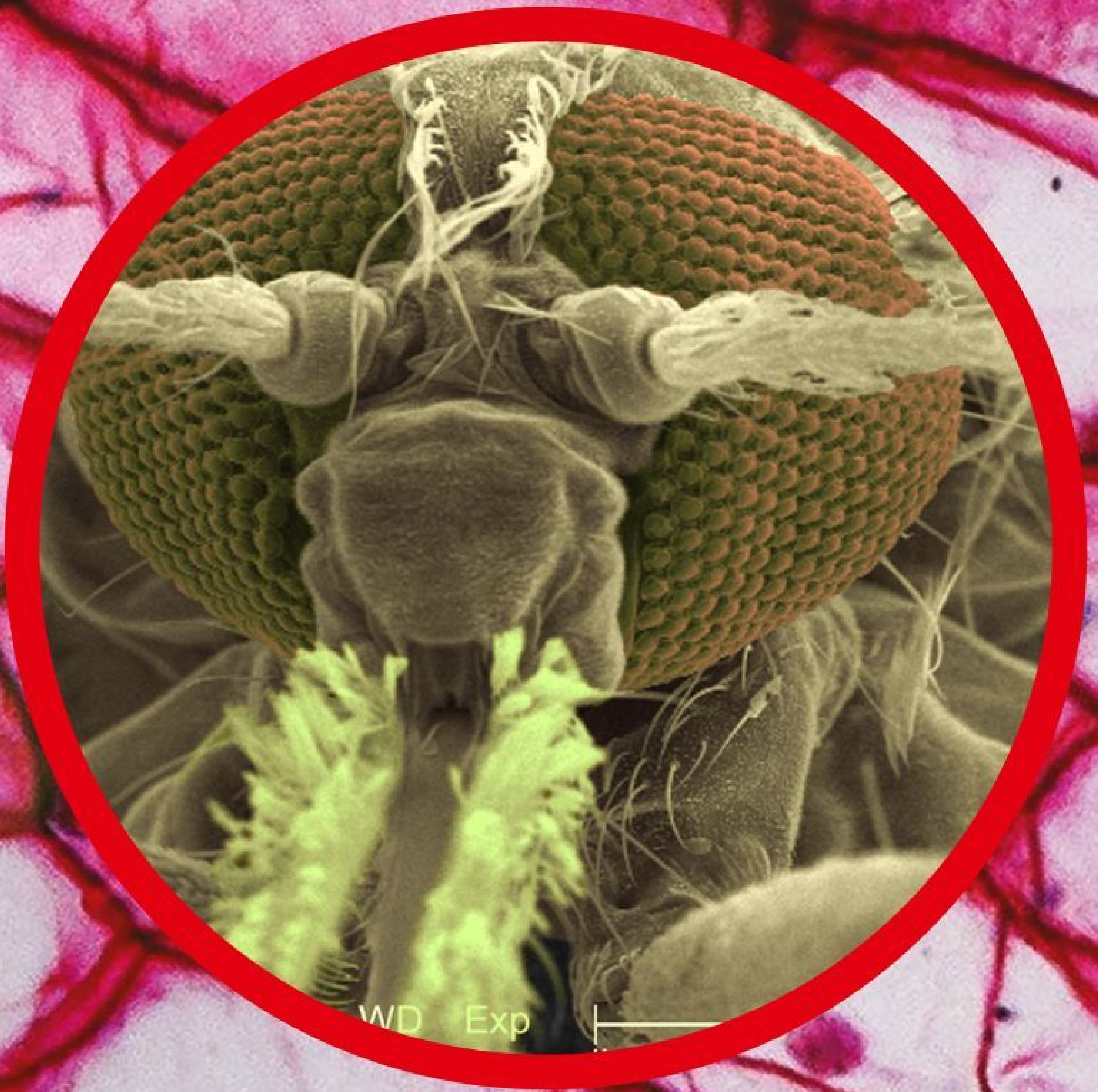
Senescence is a pre-programmed state that cells can trigger if they've started to go wrong. It puts them safely into rest mode, where they can no longer make copies of themselves, preventing more faulty cells appearing inside the body. Not only does this keep organs and tissues working as normal, it also helps to protect against cancer. One of the hallmarks of cancer cells is that they ignore instructions to stop dividing and carry on replicating forever.

Senescence also happens to young, healthy cells, and it plays an important role in growing embryos. Halting cell division in certain places, while allowing it to continue elsewhere, helps to shape the body as it develops.

○ Senescence helps to stop old cells from passing on faulty DNA

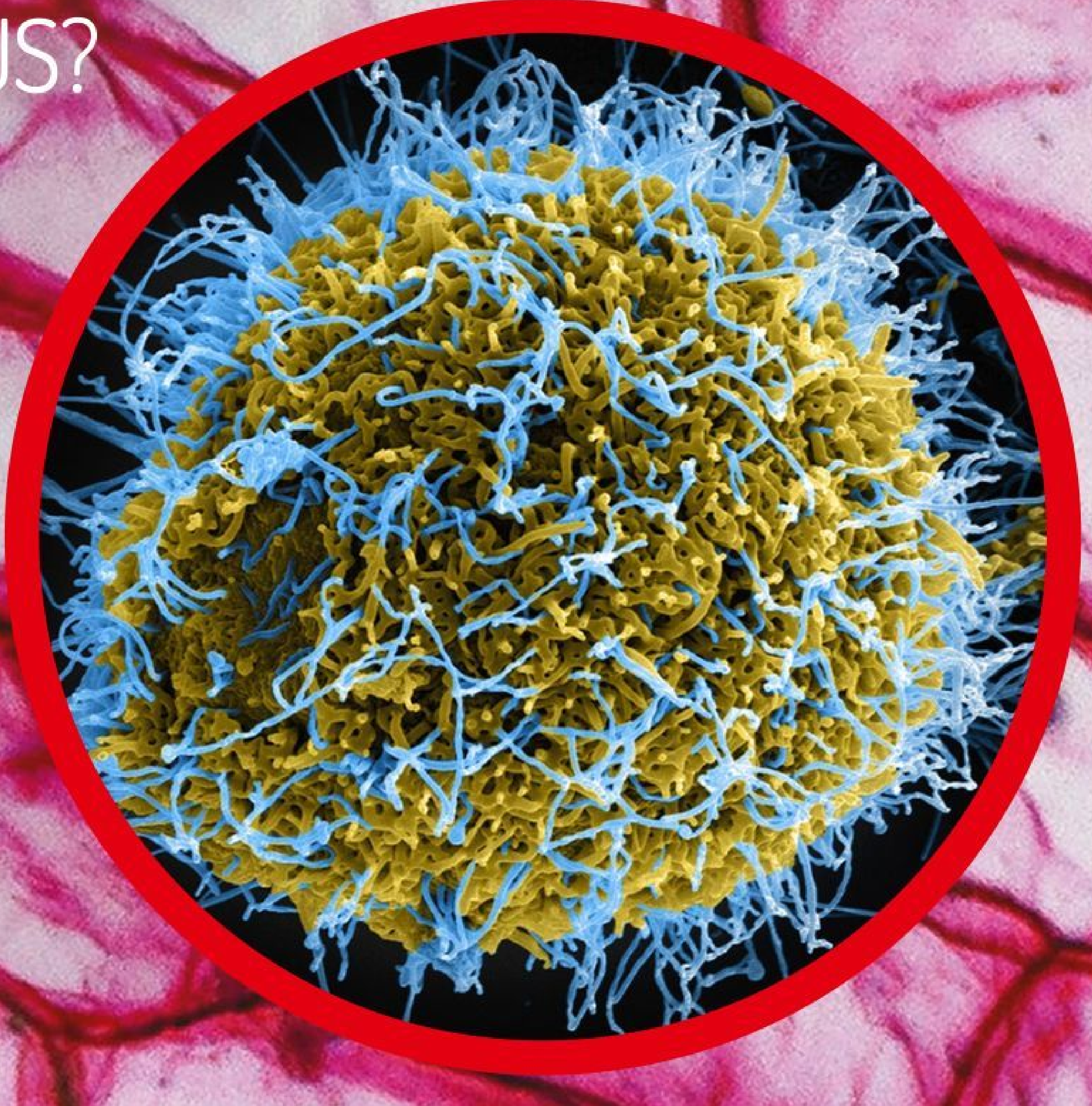
© Getty; Illustration by Ed Crooks





SMALL SCIENCE

HOW HAVE MICROSCOPES REVEALED THE TINY WORLD AROUND US?



What is the smallest thing you can see? A grain of sand? The lines of your fingerprints? Or perhaps, if you look really closely, the diameter of a human hair? Throughout most of human history, our eyesight was one of the biggest limitations on scientific research. Because we couldn't see cells or bacteria or atoms, we had no concept of these things, and it wasn't until the invention of the microscope in the 17th century that we started to understand the invisible world around us.

Scientists started to discover germs swarming in drinking water and miniature animals in lakes, and later they began to learn more about our own anatomy, finding taste buds and blood cells. Over the next century microscope technology boomed. Scientists worked to develop microscopes that were powerful enough to help diagnose cancer, seek out evidence at crime scenes, and, later in the 19th century, discover the building blocks of everything in our universe – atoms. From the humble beginnings of the simple microscope to the development of the first electron microscope, today we have far more advanced technology that can even view the space between atoms.

Microscopes are used to view and photograph very small objects that are invisible to the human eye. They can be categorised into two large groups: optical and electron. Optical microscopes are the ones you probably think of when you think of a microscope – they use a light source and a series of magnifying lenses so you can investigate your sample. This broad category is often used in diagnostic medicine and includes fluorescence microscopy, which observes fluorescence emitted by samples under special lighting, and laser microscopy, which uses laser beams to visualise samples.

Electron microscopes are even more complex, offering higher magnification and resolution. Instead of a beam of light, these pieces of equipment use a beam of electrons to create a projected image or record the bouncing back of electrons from the sample. There is also scanning probe microscopy, which includes atomic force microscopes that scan the surface of samples using a pyramid-shaped probe to map the surface of the specimen.

> *"IT WASN'T UNTIL THE INVENTION OF THE MICROSCOPE IN THE 17TH CENTURY THAT WE BEGAN TO UNDERSTAND THE INVISIBLE WORLD AROUND US"*

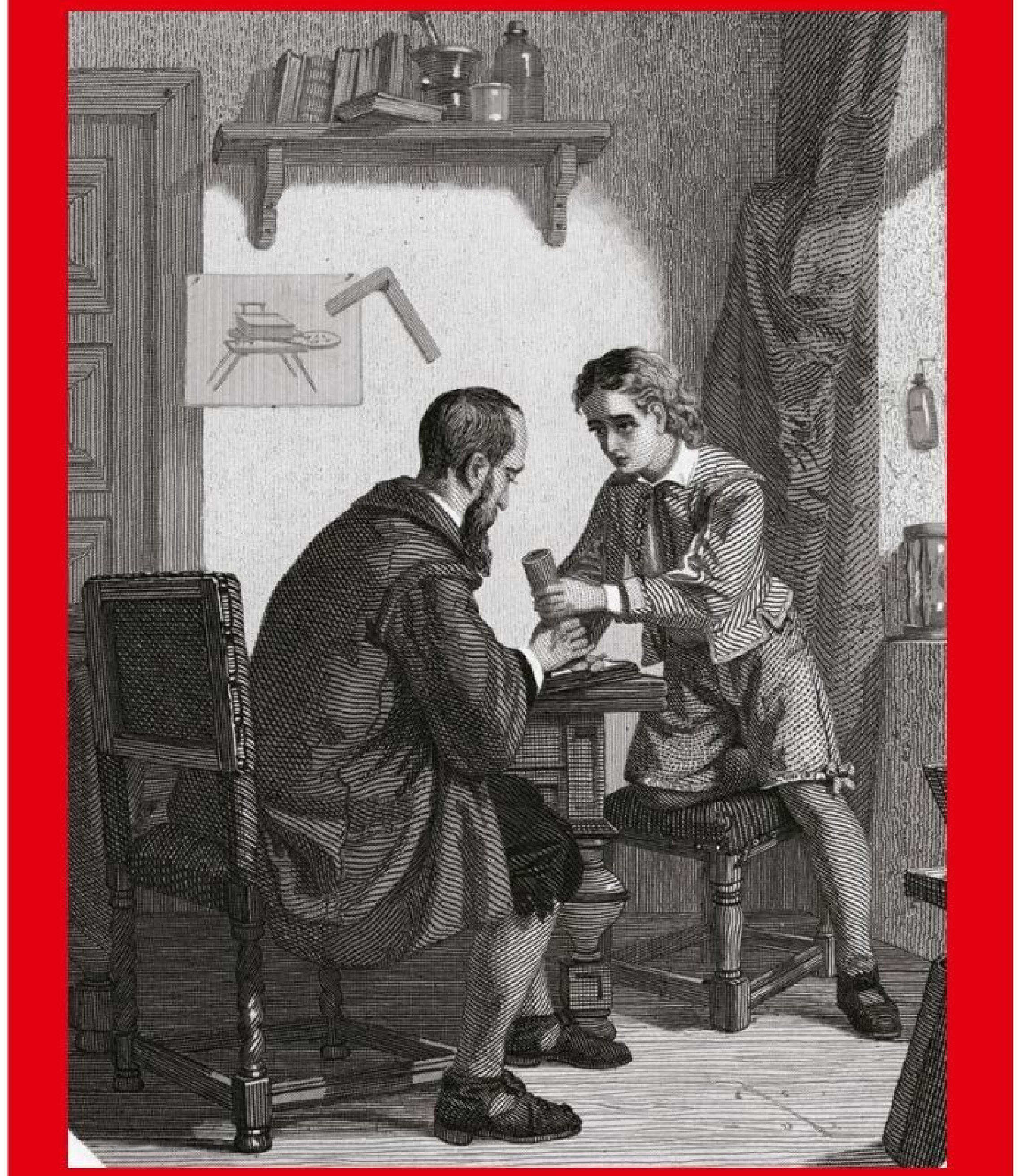
WHY DO WE NEED ELECTRON MICROSCOPES?

When you are looking at something really small, if you have enough light your eyes can distinguish two points that are about 0.2 millimetres apart. This means the resolution of your eyes are about 0.2 millimetres. Light microscopes have much better resolution, and electron microscopes even more so. This is

WHO INVENTED THE MICROSCOPE?

Like many inventions, trying to work out who was the first person to build a microscope isn't very simple. Historians are undecided on if it was Hans Lippershey (the person who patented the first telescope) or the father-son spectacle makers Hans Martens and Zacharias Janssen. All three lived in the same town in Middelburg, Netherlands. These first microscopes were quite simple; they were just a tube with a lens placed at each end but could achieve up to 9x magnification.

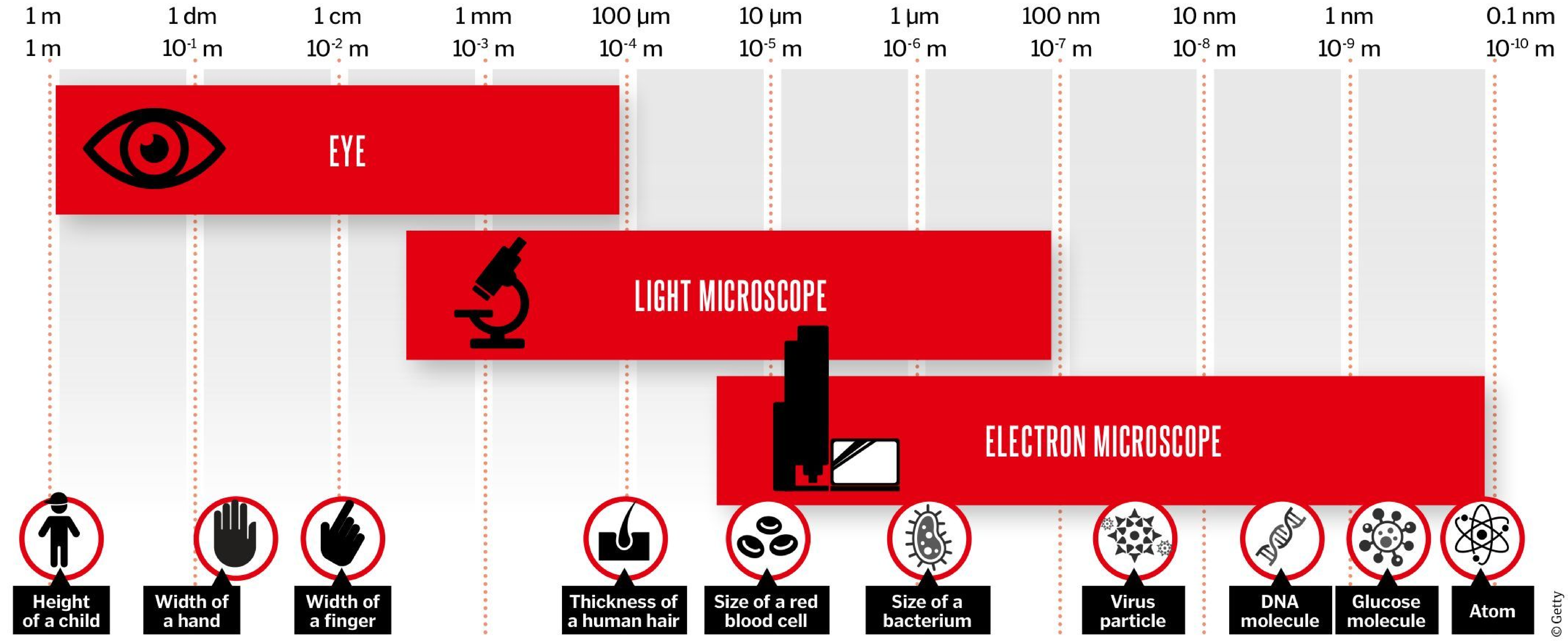
While Zacharias Janssen and his father claimed that Lippershey stole the idea from them, a view that was backed up by letters from the Dutch diplomat Willem Boreel, Zacharias was known to be a dishonest character who made a fortune from forging coins.



○ Hans Martens and his son Zacharias using an early microscope

UNDER THE MICROSCOPE

NOT EVEN ATOMS CAN ESCAPE THE GLARE OF THESE TOOLS



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> “A HIGH-VOLTAGE ELECTRICITY SUPPLY POWERS THE CATHODE, WHICH GENERATES A BEAM OF ELECTRONS”

because electrons have much shorter wavelengths than white light, which has wavelengths of about 400 to 7,000 nanometres. The beams of electrons in an electron microscope are nearer 0.1 nanometres. The smaller wavelength means less diffraction of light being scattered in random directions and as a result a less ‘fuzzy’ and more precise image.

As scientists learn more about the microscopic world and our technology gets smaller, many structures of interest to research cannot be observed with light microscopy any longer. We require higher power and higher resolution to create things such as the tiny microchips inside our smartphones, and electron microscopes are becoming more popular.

MICROSCOPES IN DIAGNOSTICS AND CRIME SCENES

While technology relies on electron microscopes, many fields of biology are reliant on optical microscopes, particularly when it comes to identifying disease. Researchers use optical microscopes in diagnostics to observe samples. This is because diseases often leave a path of specific changes to the cells that can give a clue as to what is happening to a patient, such as the trademark dark dots inside malaria-infected cells.

Optical microscopes are also utilised a lot in the field of forensics, where investigators diligently search for even the tiniest clues left at a crime scene and need to magnify evidence such as fingerprints or fibres from clothing.

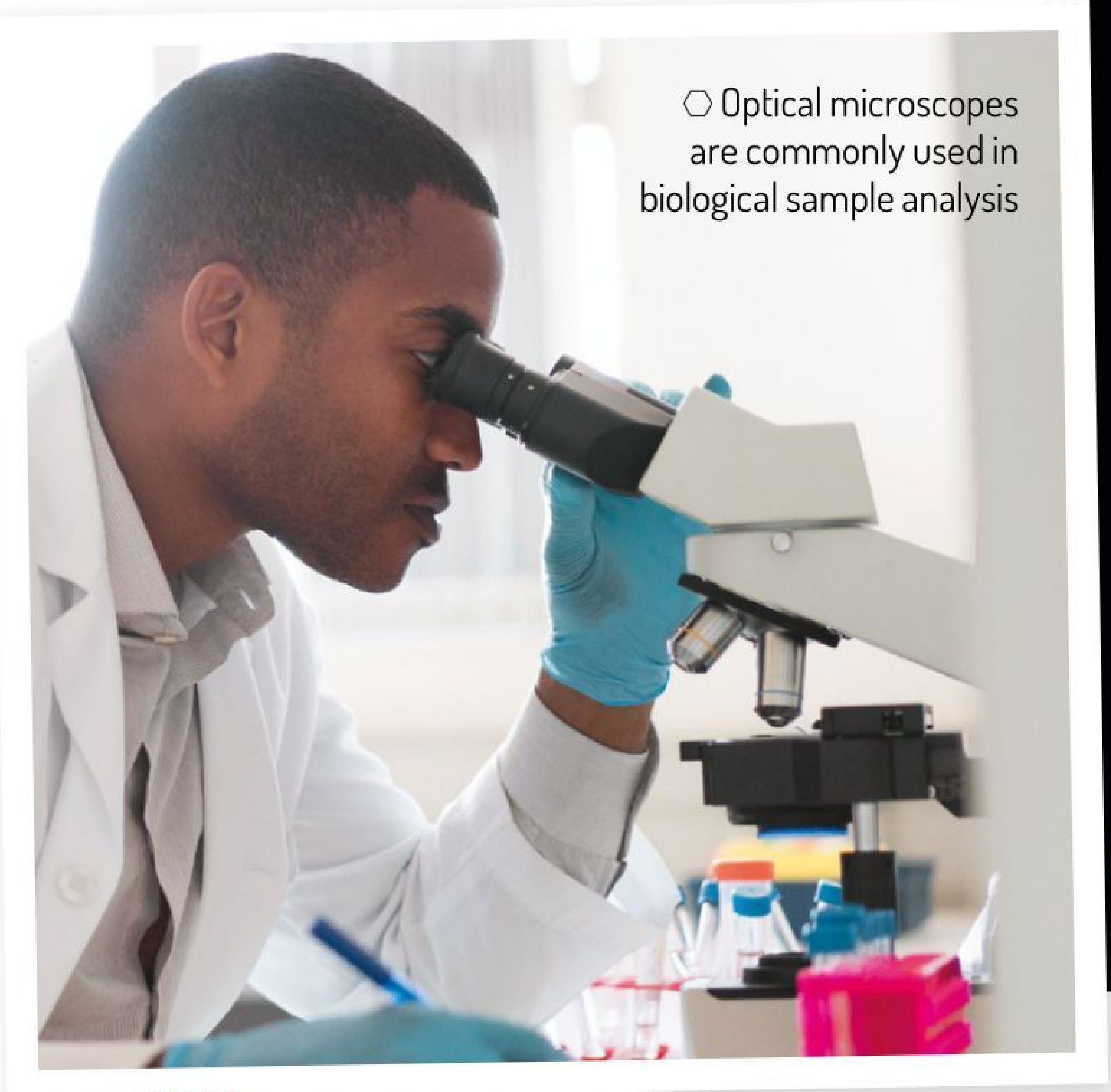
Electron microscopes can't take coloured photographs but they can be coloured artificially, like this image of red blood cells

THE FUTURE OF MICROSCOPES

There are many ideas and inventions that were created over the last decade that are still being developed for use in industry. At the forefront of pioneering work to improve microscope technology is the University of Manchester. Teams there have helped to develop a record-breaking optical microscope that has brought biologists a step closer to being able to view live viruses (which currently can only be viewed under an electron microscope).

Another project, launched by the University of York, aims to combine the technology from optical and electron microscopes into one system in an attempt to overcome the challenges associated with both types.

It might be hard to predict the technologies of the future, but one thing we can be certain of is microscopes haven't yet reached their full potential. Who knows what we will discover?



Optical microscopes are commonly used in biological sample analysis

FIVE THINGS SCIENTISTS HAVE DISCOVERED THANKS TO MICROSCOPES

1. BACTERIA

Antonie van Leeuwenhoek discovered bacteria and protozoa swarming in water during the late 1670s. He sent beautifully detailed drawings of them to the Royal Society in London.

2. CELLS

Plant cells were discovered by Robert Hooke in 1665. He was looking at dead cells from cork and named them ‘cells’ because he thought they resembled ‘cellula’ (the small rooms in monasteries).

3. ATOMIC NUCLEUS

In the Geiger–Marsden experiments, scientists discovered that atoms contain a positively charged nucleus where most of its mass is concentrated. They did this by watching for the glow of alpha particles with a microscope.

4. HUMAN GENES

In 1995, scientists Edward B Lewis, Christiane Nüsslein-Volhard and Eric Wieschaus found the genes involved in human development.

5. SICKLE CELL ANAEMIA

In 1910 intern Ernest E Irons discovered the painful inherited condition sickle cell anaemia after he performed blood work on a student who had anaemia with odd crescent-shaped red blood cells.

BIG MICRO MOMENTS

MICROSCOPES HAVE COME A LONG WAY

750–710 BCE
The Nimrud lens is created from a rock crystal disc with a convex shape and used for burning (by concentrating the Sun's rays) or for magnification.

1200S
Using lenses in eyeglasses becomes common practice and single lens magnifying glasses become popular.

1619
Date of earliest description of a compound microscope after Dutch ambassador Willem Boreel sees one in London belonging to inventor Cornelis Drebbel.

1655
The first record of claims that Hans Martens and Zacharias Janssen invented the compound microscope in 1590.

1665
Robert Hooke publishes a collection of biological photographs in Micrographia and pioneers the word ‘cell’ for the shapes he finds in bark.

1673
Antonie van Leeuwenhoek improves the simple microscope in order to see biological samples. He later observes bacteria.

MEET THE MICROSCOPES

THESE MACHINES USE DIFFERENT TECHNIQUES TO LET US SEE SOME OF THE SMALLEST OBJECTS IN OUR UNIVERSE

OPTICAL MICROSCOPES

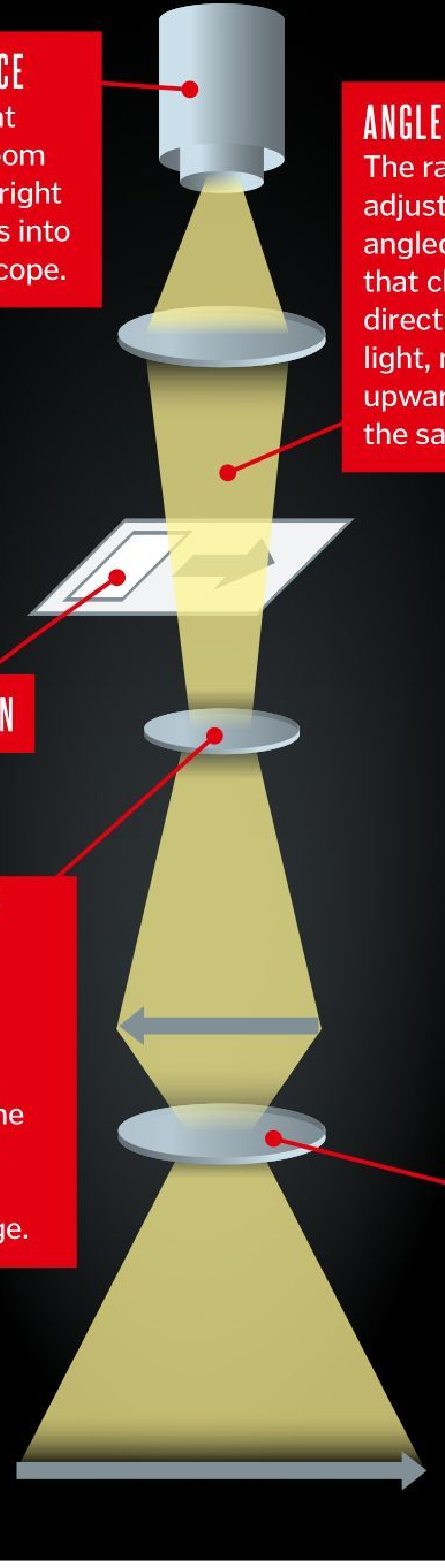
Optical microscopes use light and a series of magnifying lenses to view specimens such as blood or tissue cells. They're probably the sort of microscope you used during science class at school. While they are the oldest microscope design, they remain vital in biological research and medical diagnostics.

ADVANTAGES

- Researchers can see the natural colour of the sample.
- Samples can be living or dead.
- Optical microscopes are not affected by magnetic fields.

DISADVANTAGES

- The preparation to make a sample may distort specimen.
- Magnification is limited to 1500x.
- The resolving power (the distance needed to distinguish two points) for biological specimens is only around 1nm.



LIGHT SOURCE
Natural light from the room or from a bright lamp shines into the microscope.

ANGLED MIRROR
The rays hit an adjustable angled mirror that changes the direction of the light, moving it upwards toward the sample.

SPECIMEN

OBJECTIVE LENS
Light from the mirror passes through the sample on the slide and hits the objective lens, illuminating a magnified image.

EYEPIECE LENS
The eyepiece lens further magnifies the sample from the objective lens.

SCANNING ELECTRON MICROSCOPES

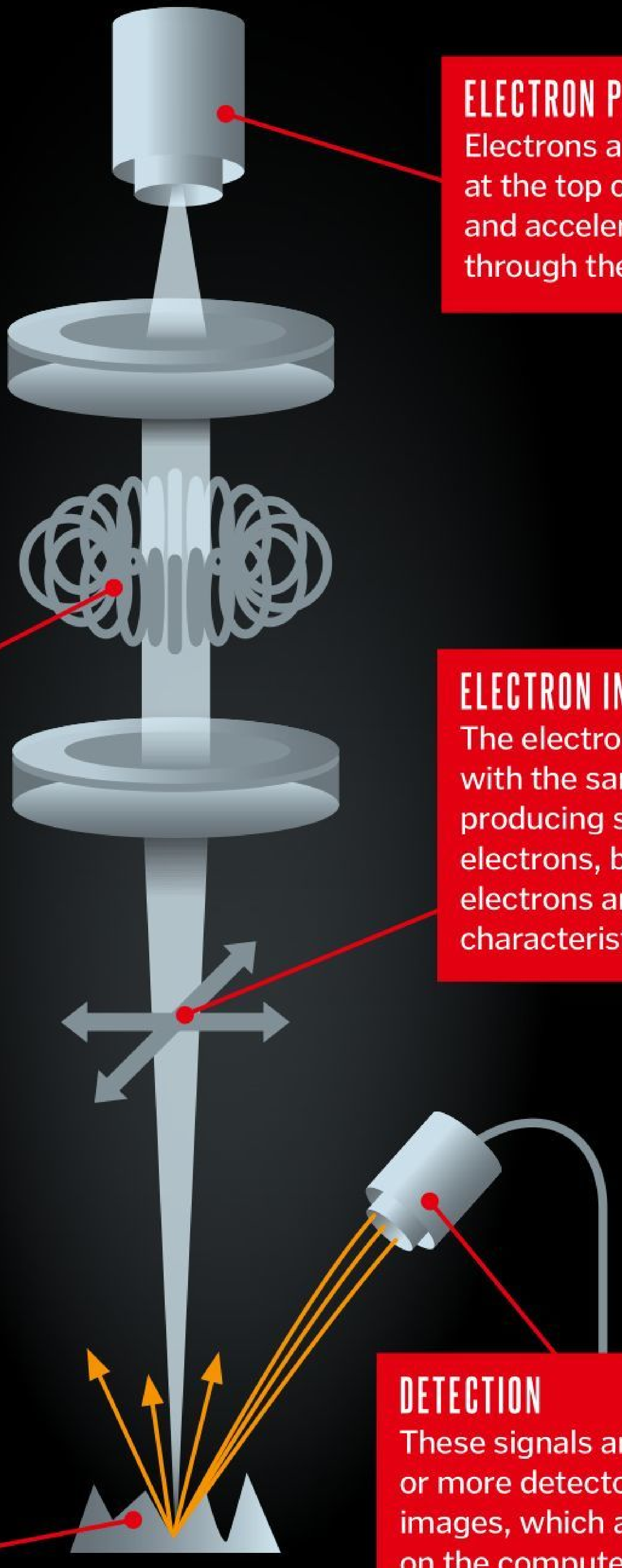
Scanning electron microscopes use a beam of electrons that are scanned over the surface of a sample, which causes the production of secondary electrons, backscattered electrons and characteristic X-rays. These microscopes are held in vacuum chambers to prevent the electrons from hitting air molecules, and modern full-sized SEMs can provide a resolution between 1–20nm.

ADVANTAGES

- Minimal preparation of samples is required.
- Can provide detailed, three-dimensional and topographical imaging.
- Works fast and provides images within minutes.

DISADVANTAGES

- Samples must be solid and able to tolerate vacuum pressure (not suitable for biological samples).
- Risk of radiation exposure due to the scatter of electrons from beneath the sample.
- Complicated and expensive, they are large and sensitive to electrical, magnetic and vibrational interference.



ELECTRON PRODUCTION
Electrons are produced at the top of the column and accelerated down through the microscope.

FOCUSED BEAM
Electrons pass through a combination of lenses and apertures to produce a focused beam.

ELECTRON INTERACTION
The electrons interact with the sample, producing secondary electrons, backscattered electrons and characteristic X-rays.

DETECTION
These signals are collected by one or more detectors to form images, which are then displayed on the computer screen.

SPECIMEN

TRANSMISSION ELECTRON MICROSCOPE

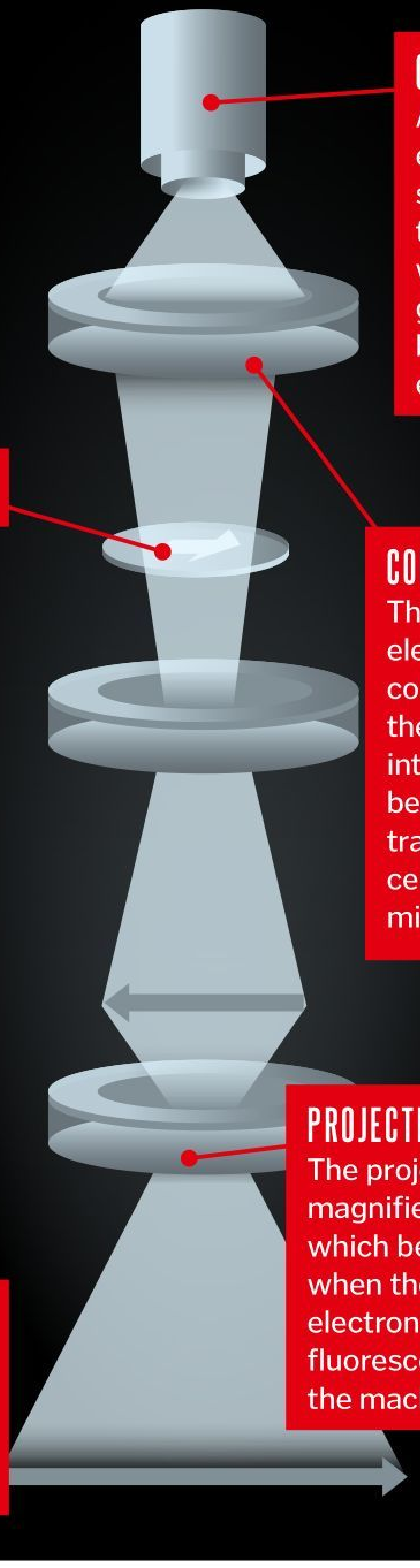
Transmission electron microscopes are the most powerful microscopes we have today. The electrons pass through the sample and are focused to form an image on a screen or onto a photographic plate. The faster the electrons hurtle down the microscope, the smaller the wavelength and the more detailed the image.

ADVANTAGES

- The most powerful microscopes, they can magnify by over 1 million times.
- Provide information on the element and compound structure of samples.
- Can determine shape and size as well as structure and surface features.

DISADVANTAGES

- Samples must be 'electron transparent' (a thickness less than 100nm).
- Images are composed in black and white.
- Preparation of specimen is difficult and complex.



CATHODE RAY
A high-voltage electricity supply powers the cathode, which generates a beam of electrons.

SPECIMEN

CONDENSER LENS
The first electromagnetic coil concentrates the electrons into a powerful beam that travels down the centre of the microscope.

PROJECTION LENS
The projector lens magnifies the image, which becomes visible when the beam of electrons hits a fluorescent screen at the machine's base.

1873
The Abbe sine condition is discovered by Ernst Abbe, a requirement that a lens needs to satisfy if it is to form a sharp image that is free of any distortions.

1951
The field ion microscope is invented by Erwin Wilhelm Müller, making viewing atoms possible for the first time in history.

1953
Professor of theoretical physics Frits Zernike receives Nobel Prize for inventing the phase-contrast microscope.

1967
Erwin Müller builds on his original field ion microscope and creates the first atom probe, which allows the chemical identification of individual atoms for the first time.

1991
The use of the Kelvin probe force microscope is first published. It's able to observe atoms and molecules.

2008
Lawrence Berkeley National Laboratory installs a new $27-million microscope with a resolution of half of an angstrom. It remains the most powerful microscope to date.

© Getty

SUPER STEM UK

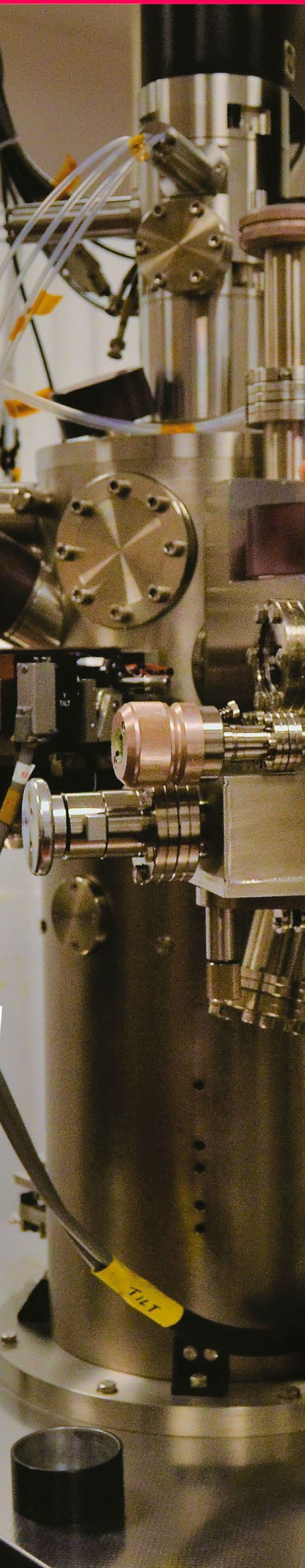
A LABORATORY IN DARESBURY HOSTS SOME OF EUROPE'S MOST POWERFUL MICROSCOPES

Some of the most powerful microscopes in the UK can be found in the countryside town of Daresbury, Cheshire. It's home to the UK National Facility for Advanced Electron Microscopy is funded by the Engineering and Physical Sciences Research Council (EPSRC). Here, researchers from all over the world come together to use the powerful microscopes that are kept at the facility. The newest model is the Nion UltraSTEM 100MC 'HERMES', also known as SuperSTEM 3, but the institute also houses the older models Nion UltraSTEM 100 (SuperSTEM 2) and the VG HB501 microscope equipped with a Mark II Nion Cs corrector (SuperSTEM 1).

These microscopes are a specialised type of TEM called scanning transmission electron microscopes (STEM), however, the 'HERMES' microscope can be used as a conventional transmission electron microscope (CTEM) as it is fitted with additional scanning coils to allow it to switch between different modes. The STEM machines produce images by using a focused beam of electron that scans across a thin sample in a raster pattern (horizontal, almost overlapping lines across a rectangular shape). The machines are so high resolution that they require an incredibly stable environment free from vibration, temperature fluctuations and electromagnetic and acoustic waves. This sensitivity can be demonstrated by clapping near SuperSTEM 2. The interference is immediately registered on the computer and jolts the atoms to one side.

While the SuperSTEM1 requires only a basic level of stability and atmospheric monitoring, the SuperSTEM 2 is shrouded in a heavy, thick curtain to reduce interference. The SuperSTEM3 is so sensitive that it must be operated from a separate room.

The SuperSTEM facility is keen to provide access for the global scientific community. Previous projects include investigating thermoelectric oxides for power generation and looking at molybdenum disulphide, a catalyst used in oil refineries, to remove harmful sulphur impurities in fossil fuels. Researchers from all fields are invited to apply to use the microscopes in small studies free of charge pending review by the scientists at the facility.

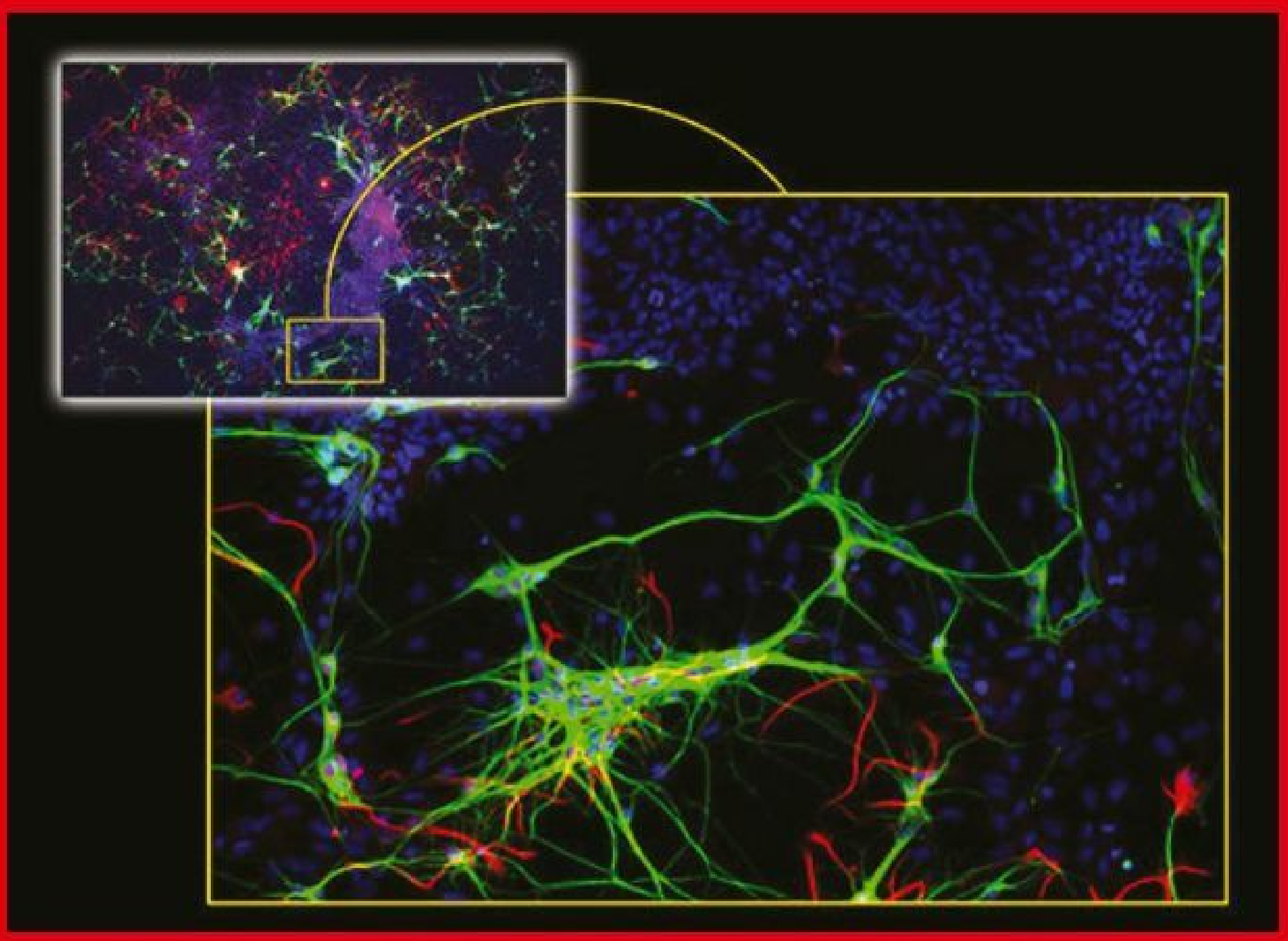


The SuperSTEM 1 is the oldest model of microscope at the facility and is an upgraded version of one of the machines built in 1970

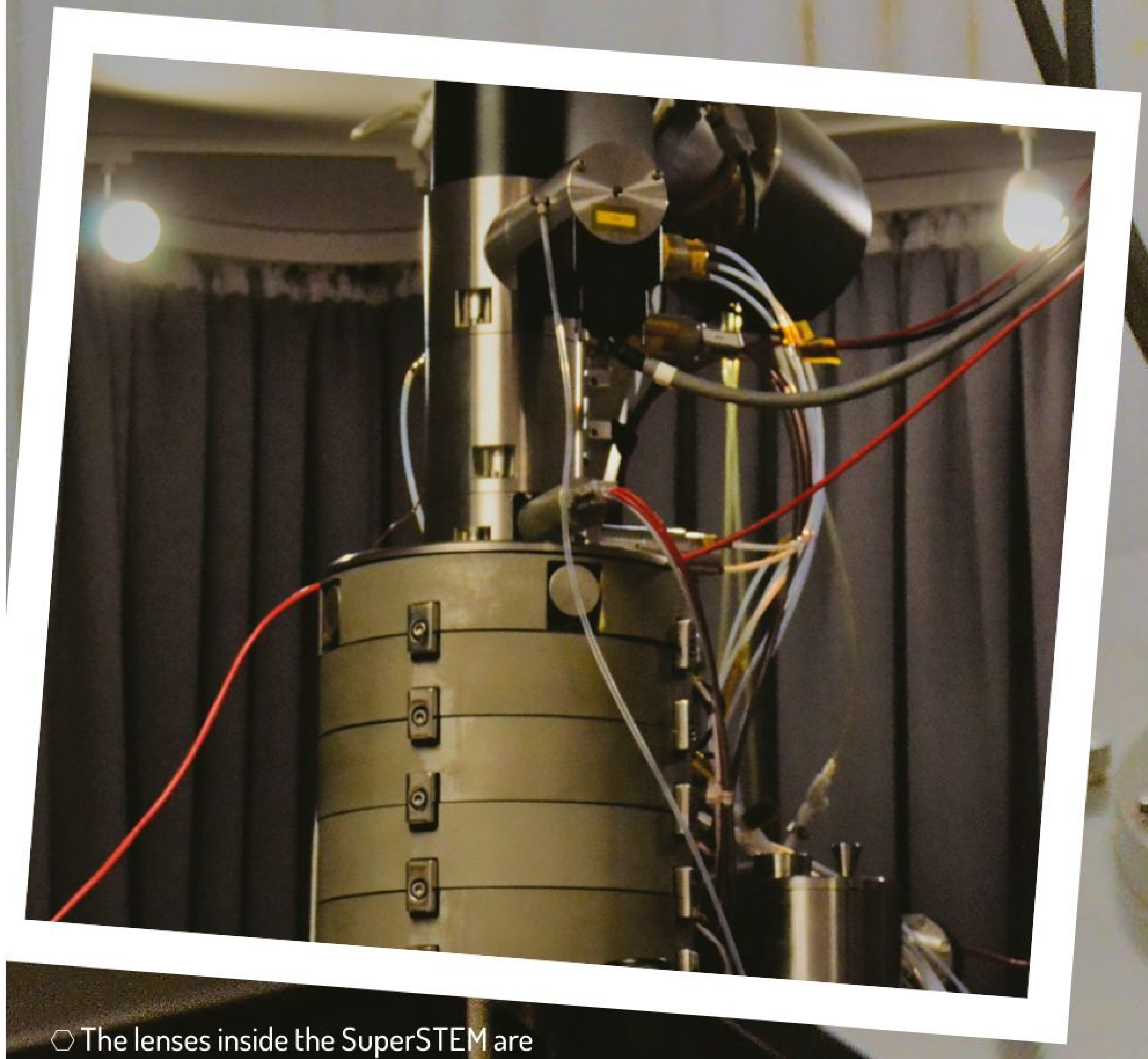
THE MESOLENS MICROSCOPE

Modern optical microscopes have to compromise between the level of detail they can provide and the amount of sample they can show at a time. The giant Mesolens was created to overcome this limitation as it is designed to have both high resolution and a wide field of view. This powerful microscope lens is able to view both densely packed cells and the entirety of an embryo in one image, and it can magnify samples by up to 4x higher detail compared to conventional counterparts that produce the same magnification.

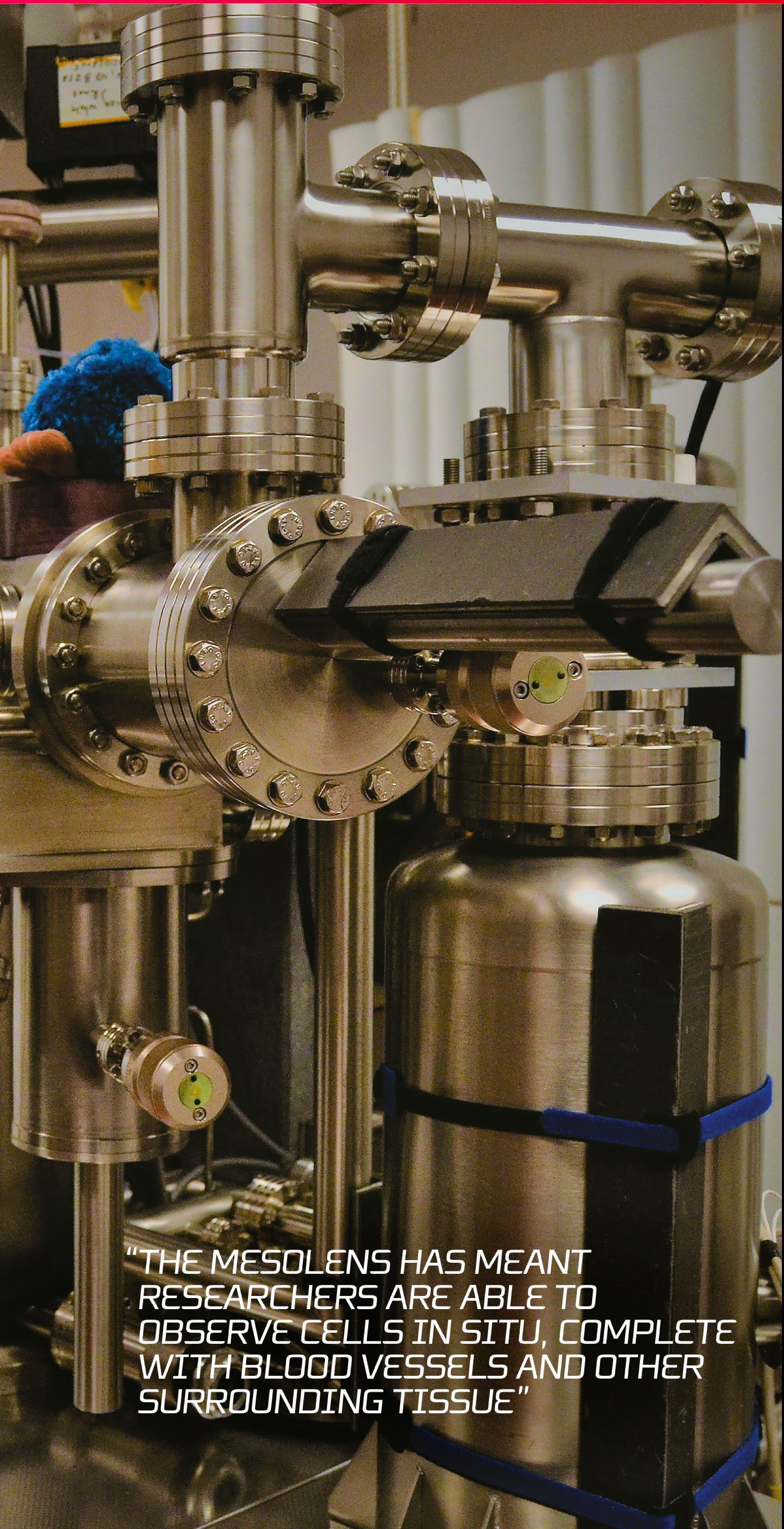
The Mesolens has meant researchers are able to observe cells in situ complete with blood vessels and other surrounding tissue and can process a volume of sample 100x greater than when using a conventional microscope.



A culture of rat brain cells stained with fluorescent dyes including neurons (green), glial cells (red) and the nuclei (blue) of astrocytes



The lenses inside the SuperSTEM are stacked to condense the beam



> "THE MESOLENS HAS MEANT RESEARCHERS ARE ABLE TO OBSERVE CELLS IN SITU, COMPLETE WITH BLOOD VESSELS AND OTHER SURROUNDING TISSUE"

AN INTERVIEW WITH SUPERSTEM'S DEMIE KEPAPTSOGLOU

HOW IT WORKS INTERVIEWS ONE OF THE SCIENTISTS BEHIND THE PROJECT TO UNCOVER THE UNIVERSE'S MANY ATOMIC SECRETS

There must have been some incredible things you've seen under these microscopes. What has been your favourite?
There's so many! Graphene, obviously. I remember the first time I looked at graphene. That was very cool because it's just a single atom thick and I was able to distinguish each atom. But also we have a collaboration with colleagues in Germany and they bring me meteorites that have travelled the universe – some of them are 4.5 billion years old. I was surprised to find out there is organic material in meteorites – there is this theory that it could be how the first organic matter came to Earth. There is a saying we have: 'We are investigating the universe, one atom at a time, but it might take us a while to get there.'

What is the importance of understanding the materials around us on an atomic level?
Do you remember the phone batteries that were exploding? These are batteries that are very, very small but are as powerful as a computer ten years ago. Obviously there was some fault in the production, but it might not have been large at all because the products are so small now. We don't realise how much work and research goes into our everyday products.

Are there any advancements that you are excited to see in the future that will need electron microscopes?
I think drug delivery systems that will involve atoms and subatomic particles. There has been research into attaching magnetic nanoparticles to drugs so that they can use a magnet to guide the drug where they need it, [towards a] tumour or something.

Are nanoparticles dangerous to our health? Can you use electron microscopes to investigate this?
Yes, I was involved in an atmospheric study and they were collecting nanoparticles on the side of the road. They were determining what kind of nanoparticles were in our air and they found a lot of iron oxides coming from the brakes of cars. Understanding what things look like and how they act is very important to understanding the impact [of small particles] on health.

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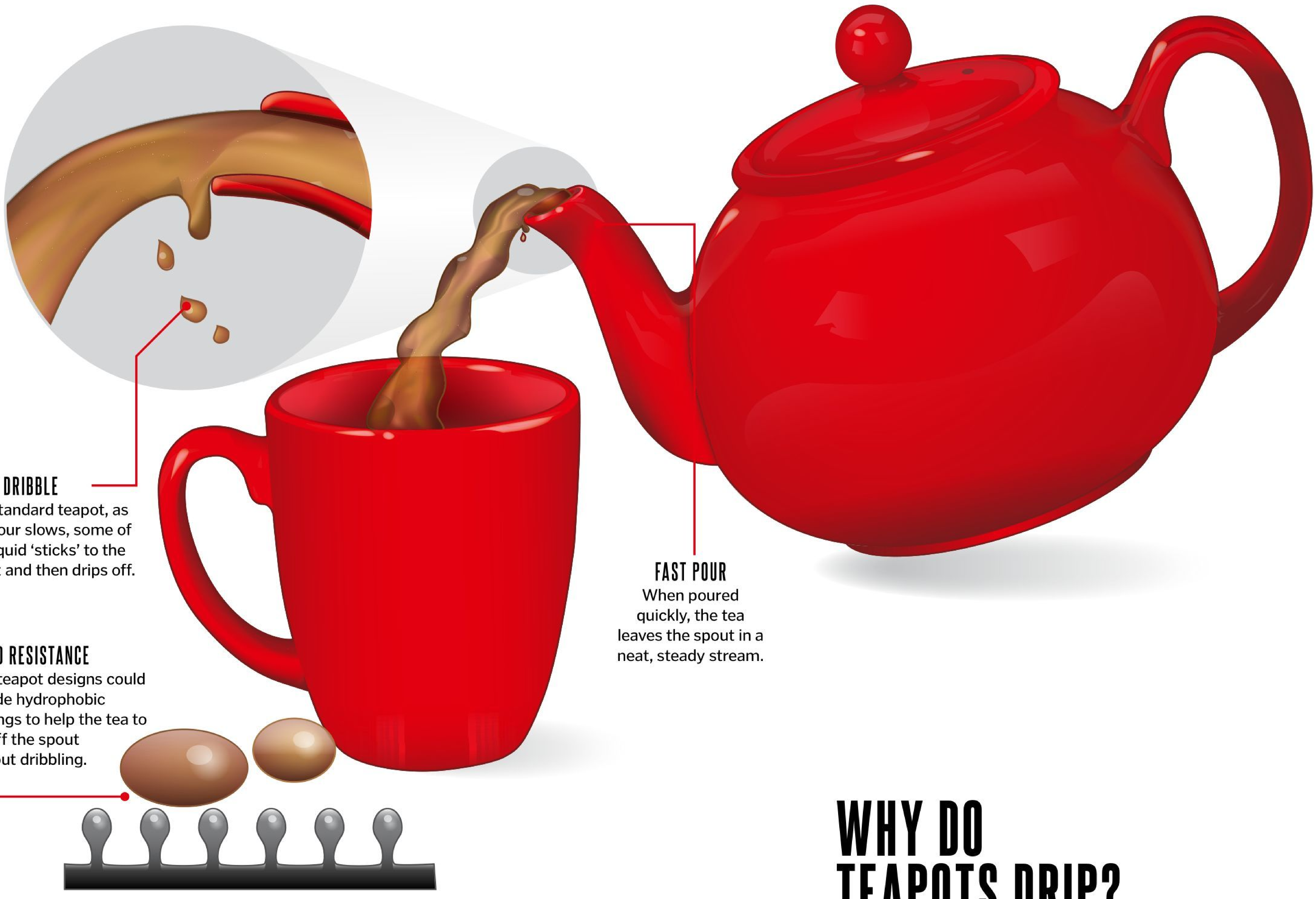
EVERYDAY SCIENCE

FROM THE MIND-BLOWING TO THE MUNDANE, WE REVEAL THE SCIENCE BEHIND LIFE'S LITTLE MYSTERIES



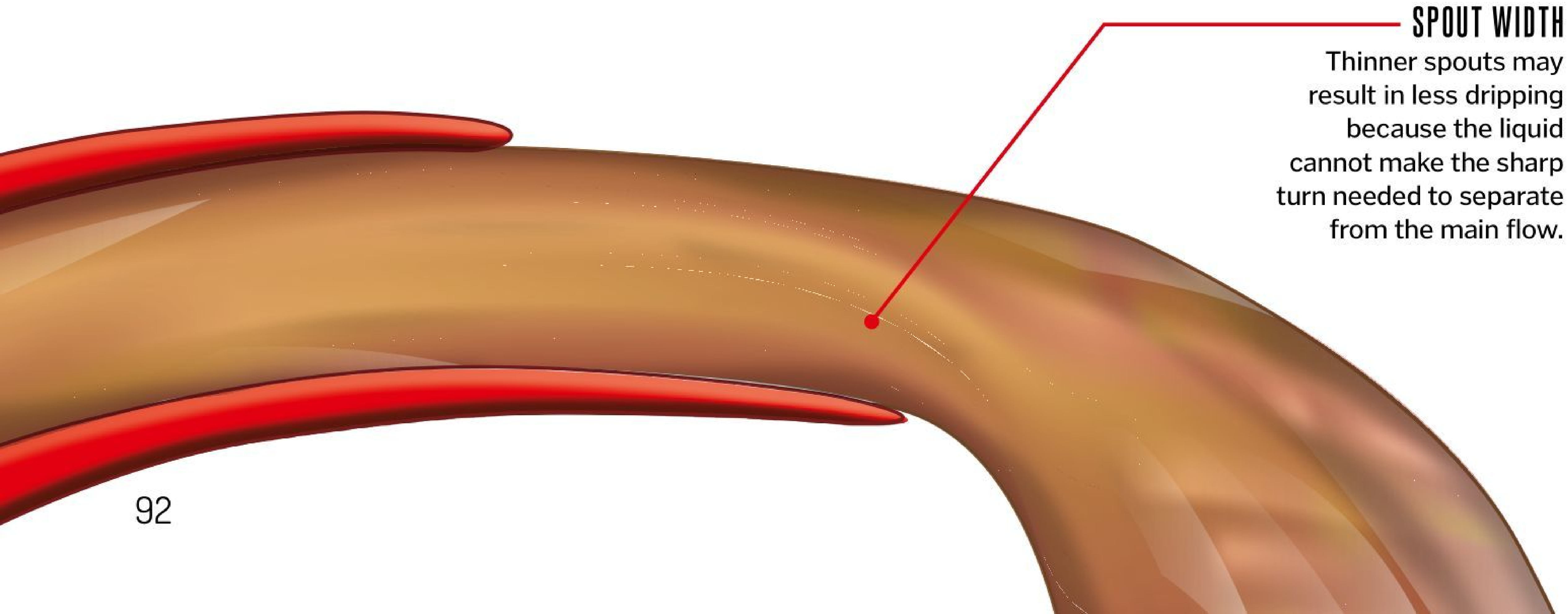
SLOW DRIBBLE
In a standard teapot, as the pour slows, some of the liquid 'sticks' to the spout and then drips off.

FAST POUR
When poured quickly, the tea leaves the spout in a neat, steady stream.

LIQUID RESISTANCE
New teapot designs could include hydrophobic coatings to help the tea to roll off the spout without dribbling.

WHY DO TEAPOTS DRIP?

Fluid dynamics researchers at the University of Lyon in France have been hard at work finding out why teapot spouts are so prone to dripping. They found that these post-pour spillages are down to the 'hydro-capillary' effect; as you pour the tea, some of the liquid tracks down the outside of the spout. This is influenced by the shape of the spout, how fast the tea is poured and how water-repellent the teapot is. Metal teapots with straight-edged spouts are much less prone to dripping than their curvy porcelain counterparts.



SPOUT WIDTH
Thinner spouts may result in less dripping because the liquid cannot make the sharp turn needed to separate from the main flow.

WHY DOES COFFEE SPILL?

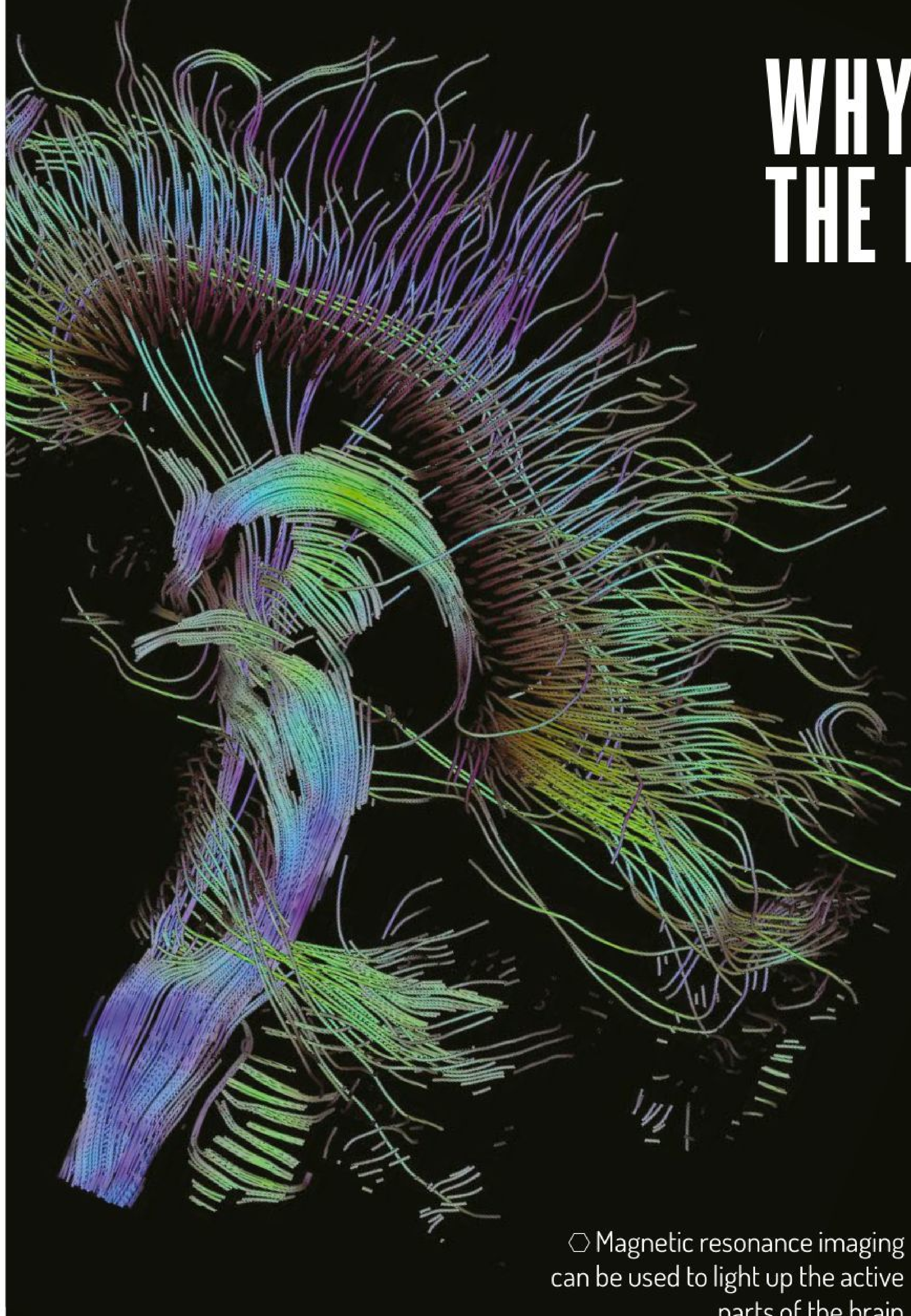
Researchers at the University of California, Santa Barbara, recorded volunteers as they carried coffee cups to expose the secret behind the spill. What they found was that it's all down to a combination of cup size, coffee fluid dynamics and the way we walk.

Fluid sloshing inside a container tends towards a natural frequency, a bit like a liquid pendulum. This varies with the size of the cup and the properties of the liquid, but for coffee in a regular mug, the natural frequency is close to walking rhythm. As you walk along, the liquid starts to sway and little irregularities in your step amplify the effect. The faster you accelerate, the more likely you are to spill.

Putting a lid on your cup can actually make things worse. As the coffee sloshes, some creeps along the underside of the lid, and climbs up the side of the cup. When these two streams collide, they shoot out of the drinking hole, creating a coffee volcano.

Researchers advise walking slowly and not filling the cup to the top

WHY DOES THE MIND WANDER?



Magnetic resonance imaging can be used to light up the active parts of the brain

The 'default mode' for the brain tends towards introspection and daydreaming, but with a bit of effort we can switch to 'focus mode' and perform complex tasks. However, if these tasks are repetitive, the mind can start to wander and we can make mistakes. The technical term for these momentary lapses is 'maladaptive brain activity changes', but colloquially they are known as 'brain farts'.

Researchers at the University of New Mexico discovered that you can spot these 'brain farts' coming a good 30 seconds before people make an error by using functional magnetic resonance imaging (fMRI), which monitors the blood flow to different parts of the brain.

IS THE FIVE-SECOND RULE REAL?

Every schoolchild has heard that if you pick food up within five seconds of dropping it, it's safe to eat, but is this an urban myth? To test the idea, researchers at the Aston University in the UK dropped toast, pasta, biscuits and sweets onto a variety of different floor surfaces and tested them for the presence of common bacteria at time points between three and 30 seconds. Bacteria do transfer before the magic five seconds is up, but generally the food is still edible. Dropping food onto carpet was better than flinging it at a hard, flat surface like laminate, and dry food fared better than wet.

Whether dropped food is safe to eat depends on the type and number of pathogens present on the floor

REWARDING IMPROBABLE RESEARCH

You might wonder why scientists are spending their time researching spilled coffee, drippy teapots and the five second rule, but these strange research projects spark people's interest in science and should be celebrated. Each year in September, ten Ig Nobel Prizes are awarded for research that makes people 'laugh, then think'. Past winners have shown how to unboil an egg, measured the friction of a banana skin and even demonstrated that asthma symptoms can be treated with rollercoaster rides.

In 2000, the Ig Nobel Prize for physics was awarded for levitating a frog in a magnetic field

© WIKI; Dreamstime; Illustration by Nick Sellers/Art Agency

WHY DOES TOAST BURN?

Toast can go from pasty white to charred and black in just a few seconds, but what is it about bread that makes it so prone to burning? The answer can be found in its chemistry.

Bread in its simplest form is made from wheat flour, yeast and water. The flour contains carbohydrates (long chains of sugars) and proteins (long chains of amino acids), and these are the key ingredients of a chemical reaction known as the Maillard reaction.

The sugars in bread (which include glucose, fructose, maltose and lactose) contain chemical groups called aldehydes (which have the formula -CHO). At temperatures above around 140 degrees Celsius, these groups start to react with the amino groups (-NH_2) found on amino acids in the wheat proteins. This is the first step in the process of turning bread into toast.

The products of these reactions are unstable and quickly rearrange into chemicals called Amadori compounds. These then go on to react even further, making a variety of colourful compounds with distinctive smells and tastes.

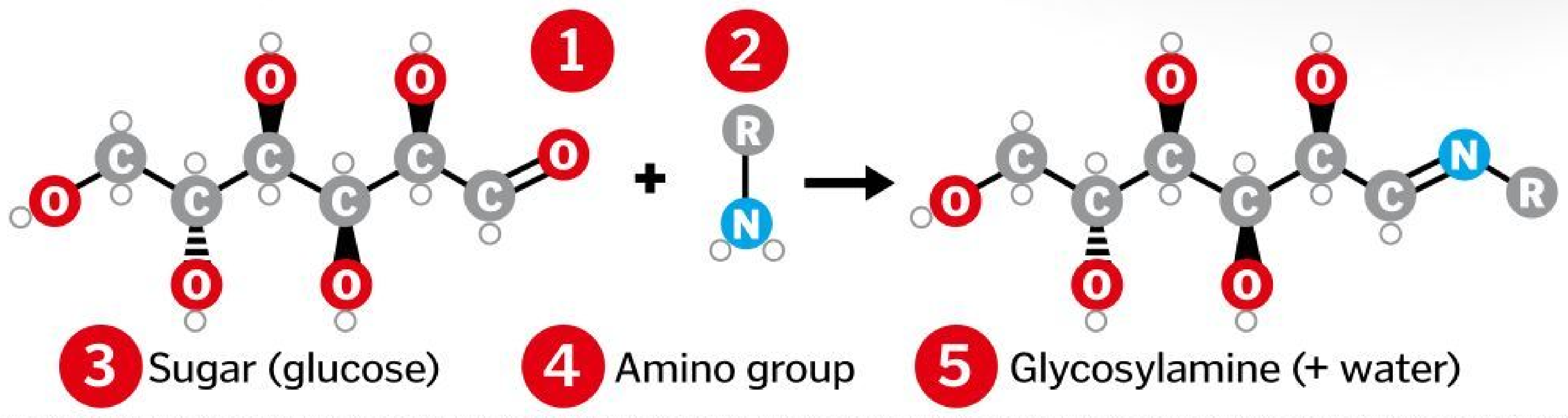
The rate at which your bread turns to toast, and then to charcoal, depends on its composition, and various sugars and amino acids produce different flavour and odour molecules when they undergo the Maillard reaction. In general, the drier the slice, the faster these reactions occur, and the quicker the toast will brown and then burn.

Alkaline breads (like those made with baking soda) should brown faster than acidic ones, and breads and buns glazed with milk or egg will colour more quickly thanks to the extra protein content on the surface.

Be extra careful when making fruit toast; the sugars will start to caramelise and will turn to crunchy carbon if left in the toaster too long.

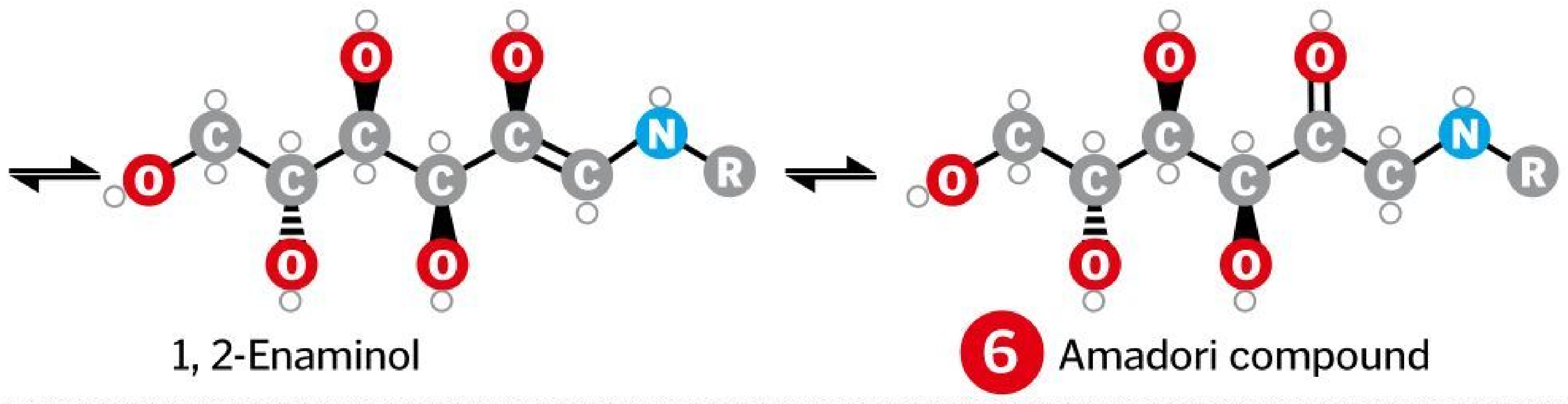
STEP 1

During the first stage of the Maillard reaction, a sugar and an amino acid combine.



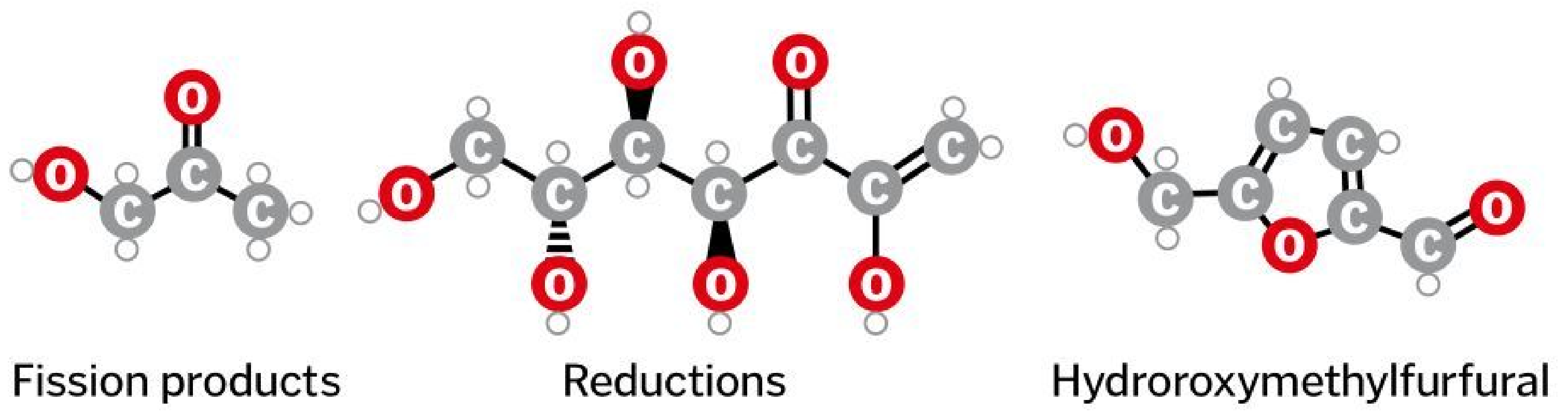
STEP 2

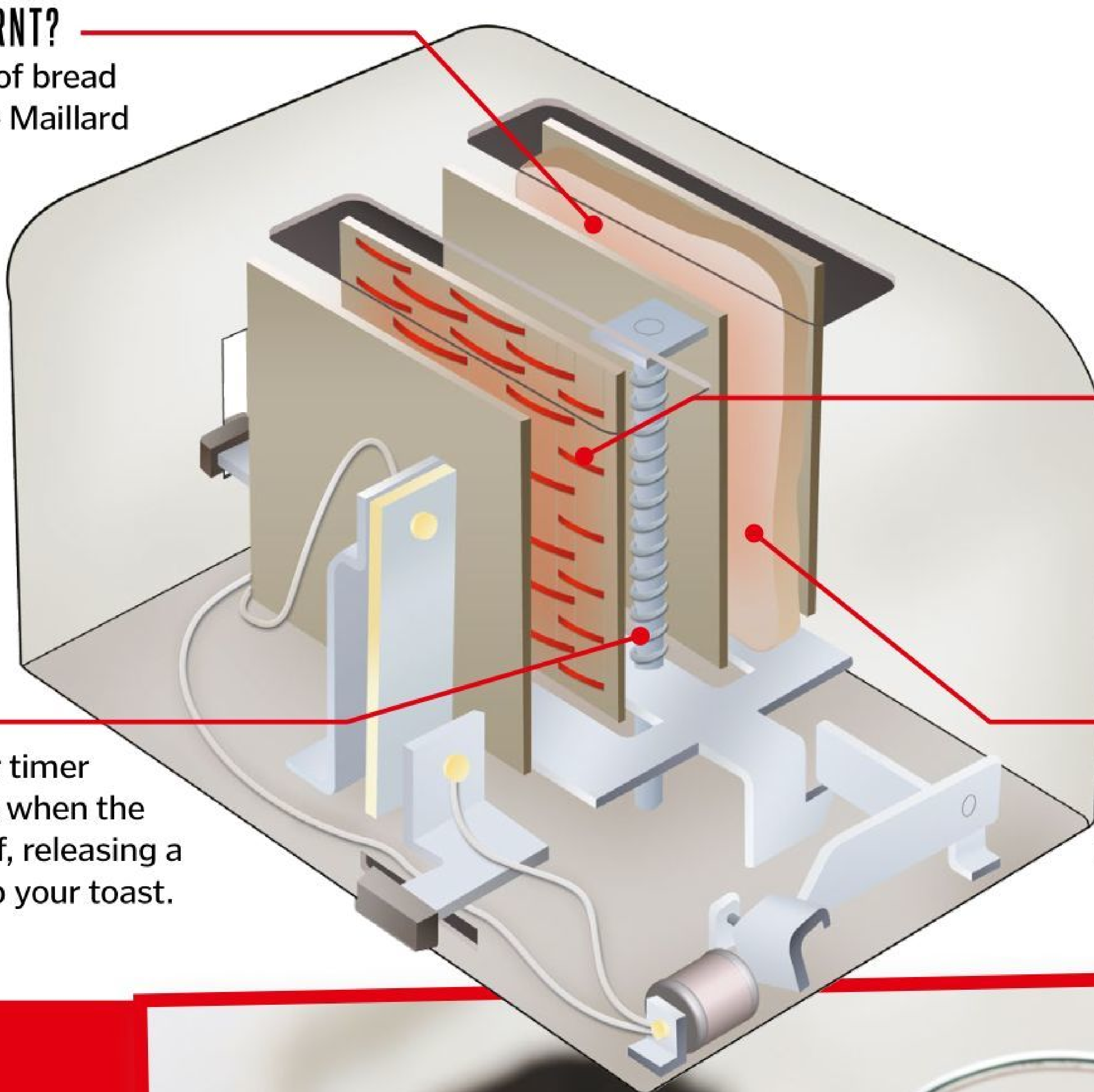
The structure made in step one undergoes rearrangement, forming an Amadori compound.



STEP 3 ⑦

The compound made in step two can undergo further reactions, producing a range of different molecules.





BROWNED OR BURNT? Different types of bread will undergo the Maillard reaction at different rates.

POP-UP A thermostat or timer usually controls when the toaster turns off, releasing a spring to pop up your toast.

FILAMENTS When an electric current flows through these thin wires, they heat up and glow red hot.

RADIATION The filaments are spaced apart and radiate heat from both sides, cooking the bread quickly and evenly.

THE TASTE OF TOAST

COMPLEX CHEMICALS ARE RESPONSIBLE FOR THE DISTINCTIVE SMELL AND TASTE OF TOAST

1 BREAD Bread contains proteins (made of amino acids) and carbohydrates (sugars).

2 HEAT At temperatures above 140°C, amino acids and sugars start to combine.

3 SUGAR The sugars found in bread include glucose, fructose, maltose and lactose.

4 AMINO ACIDS There are 20 amino acids, each with a slightly different structure.

5 GLYCOSYLAMINE Sugars and amino acids combine to form unstable compounds called glycosylamines.

6 KETOSAMINE Glycosylamines are rearranged to form ketosamines, also known as Amadori compounds.

7 PRODUCTS Various chemicals can be formed as the ketosamines continue to react.

IS IT WORTH HITTING THE SNOOZE BUTTON?

The snooze button can feel like a welcome relief, but it might be better to set your alarm later and get up right away. Your sleep goes in cycles, beginning with a couple of minutes of dozing, followed by ten to 20 minutes of light sleep, and then slipping into a longer period of deeper sleep. You cycle through these stages around every 90 minutes, and as the night goes on light sleep gives way to dreaming. It might feel good to put the alarm on snooze in the morning, but you'll already have broken the cycle, and the little bursts of light sleep won't make you feel any better when you finally kick back the duvet.

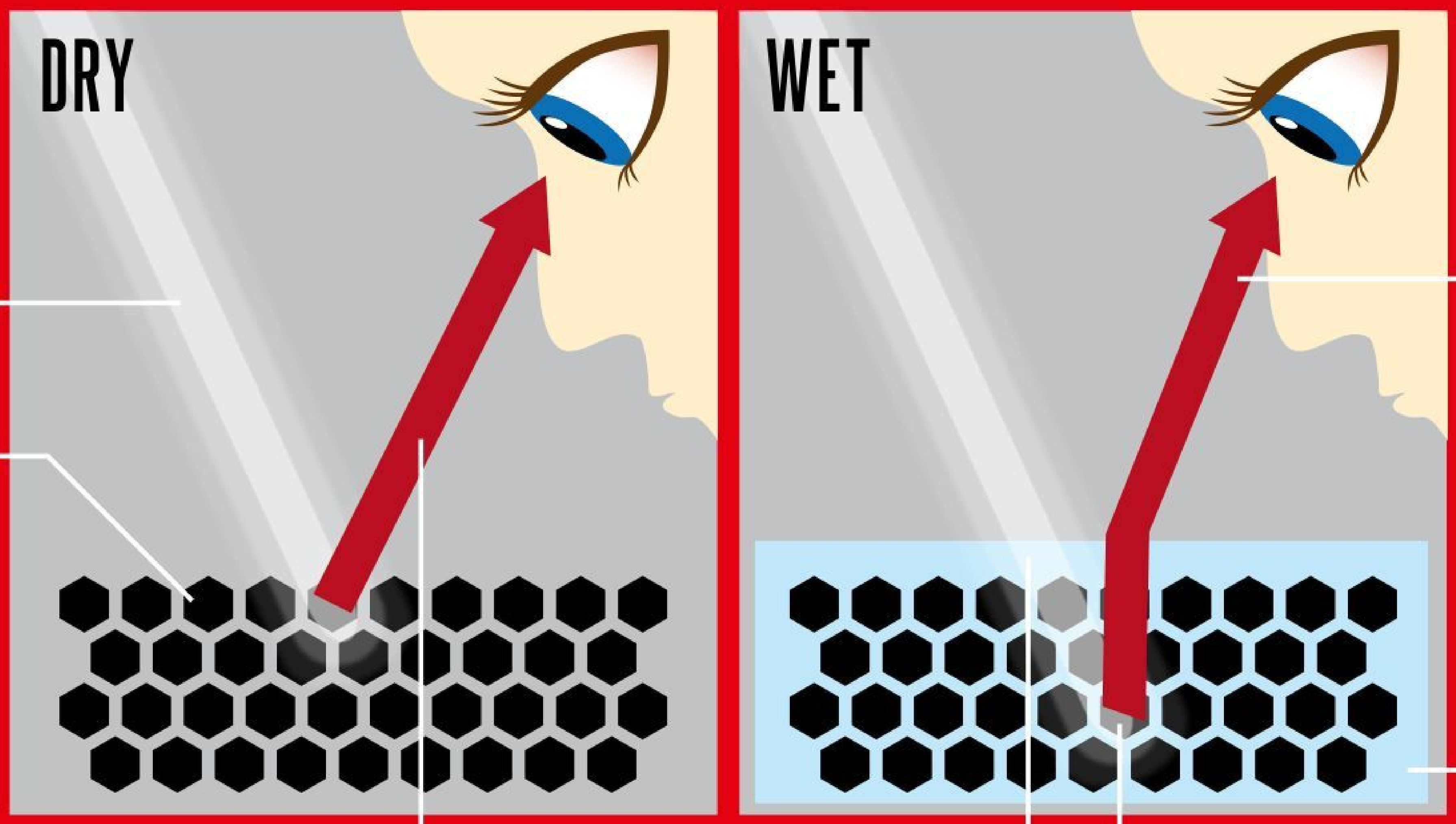
○ Forget the snooze button and enjoy your sleep uninterrupted

WHY DOES WET FABRIC LOOK DARKER?

It is easy to take this for granted, but the distinctive colour change of wet fabric is actually down to some interesting science. The amount of light reflected by a material depends on a property called the 'index of refraction', which determines how light moves through a material. When fabric gets wet, the light hitting the material has to travel through water instead of air, and this alters its path. Light moves much more slowly through water and, when it hits damp fabric, it bends. Rather than reflecting back out towards the eye, more light gets scattered within the fabric, making the colour appear darker.

WET VERSUS DRY

FIND OUT HOW WATERLOGGED FABRIC CHANGES THE PATH OF INCOMING LIGHT



INCOMING LIGHT
Incoming light strikes the dry fibres of the fabric and scatters.

FIBRES
The fibres of the fabric contain dyes and pigments that absorb certain wavelengths of light.

REFLECTED LIGHT
Some of the light is reflected by the fabric, bouncing back towards the eye.

BENT LIGHT
As light moves from air to water or water to air, its speed changes and its path bends.

TRAPPED LIGHT
Light reflected by the fibres is bent as it tries to leave the fabric.

WATERLOGGED
The gaps between the fibres of the fabric are filled with water.

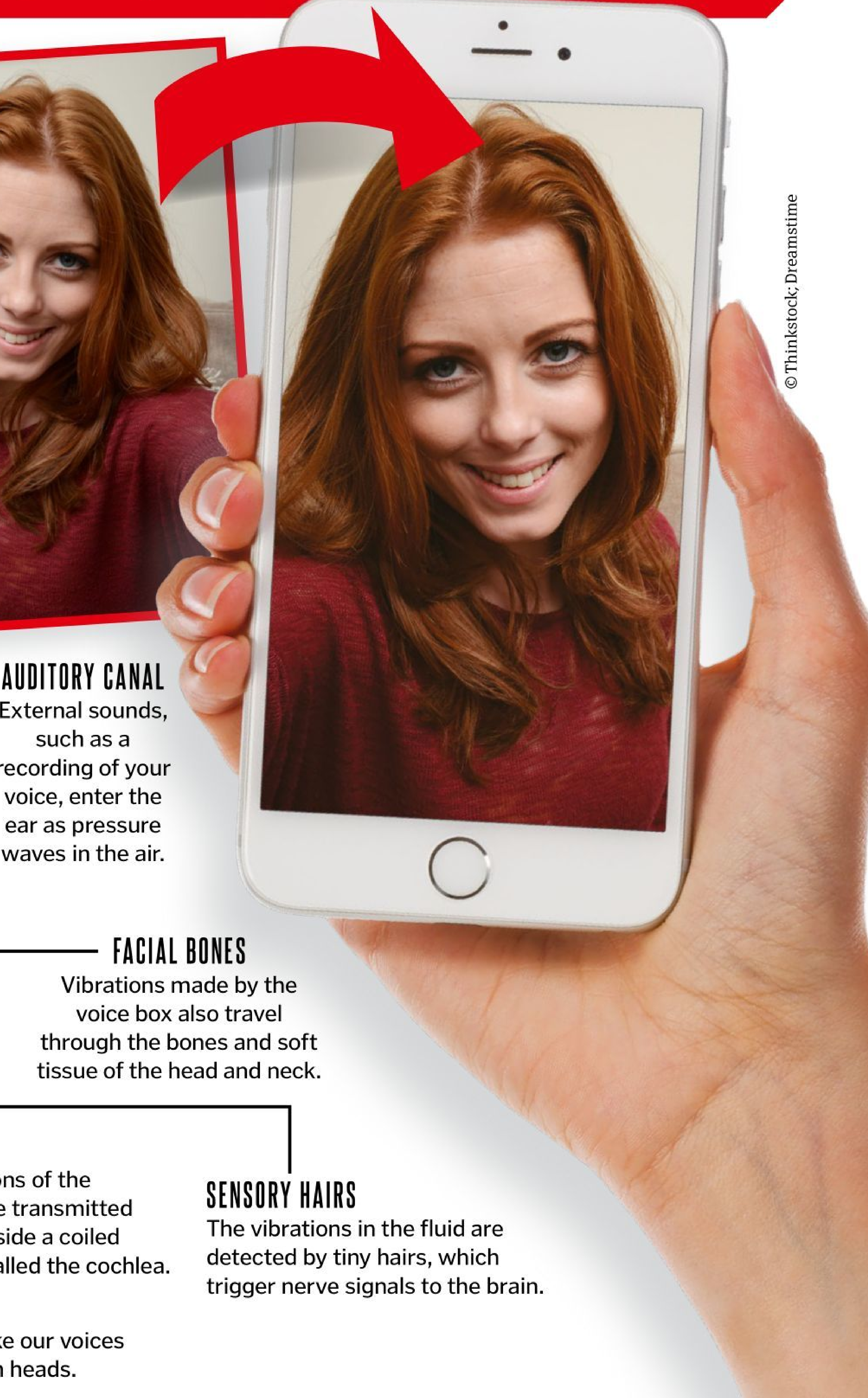
LESS REFLECTION
With less light able to escape the fabric, the fibres appear darker.

DO I REALLY LOOK AND SOUND LIKE THAT?

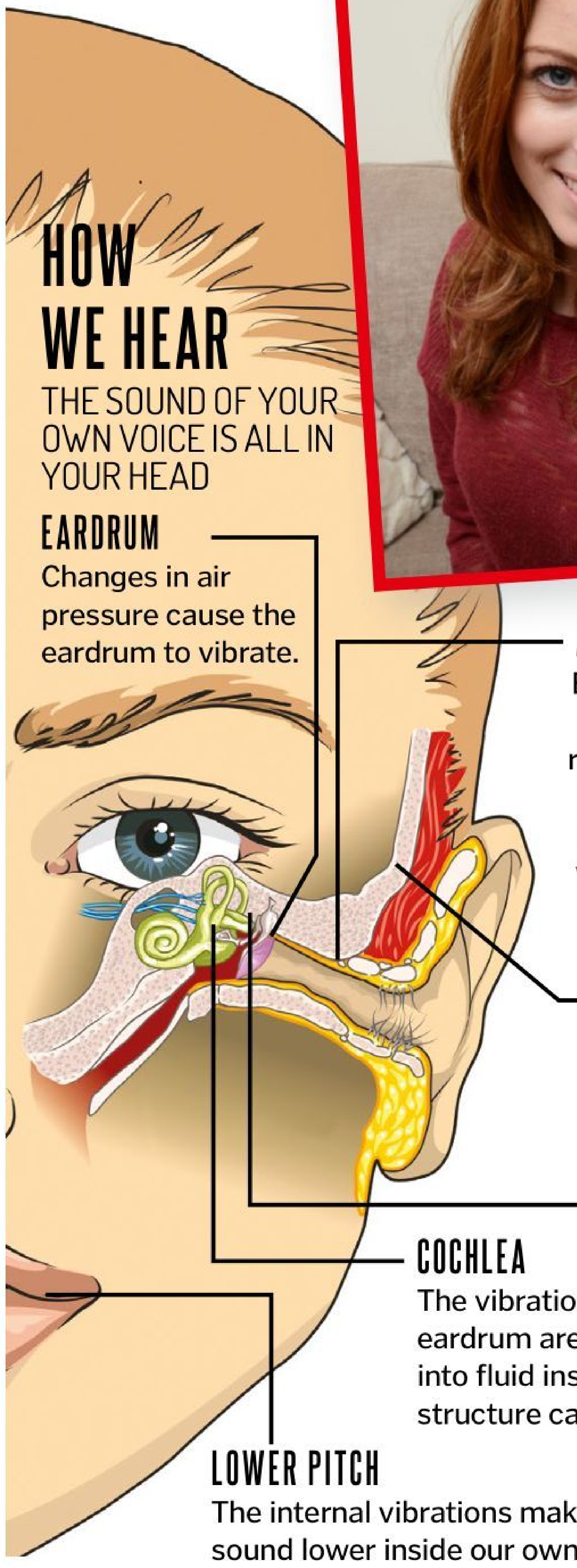
When you look in a mirror, the reflected image of yourself is a mirror image; you see yourself every single day back to front. If your face were symmetrical this would not matter, but because there are little asymmetries, it means that you mentally store a backwards picture of what you look like, and when you see your image the right way round it can look strange.

The sound of your own voice can be even stranger. When you hear someone else speaking, the sounds travel through the air as vibrations, hitting your eardrum and causing it to vibrate. This moves fluid in the inner ear, which pushes against hairs and sends signals to the brain.

When you speak, the sound reaches your ear in a different way. Not only are you picking up the vibrations in the air, you are also detecting vibrations inside your own head. As you make the sounds with your vocal cords and tongue, the soft tissues in your head and neck vibrate, and so too do the bones in your face. These additional vibrations make your voice sound lower. When you hear your recorded voice, you don't get these undertones, and the higher-pitched version of you can seem very odd indeed.



○ We are so used to seeing our mirror image that a photograph can look really strange



HOW WE HEAR

THE SOUND OF YOUR OWN VOICE IS ALL IN YOUR HEAD

EARDRUM
Changes in air pressure cause the eardrum to vibrate.

AUDITORY CANAL
External sounds, such as a recording of your voice, enter the ear as pressure waves in the air.

FACIAL BONES
Vibrations made by the voice box also travel through the bones and soft tissue of the head and neck.

COCHLEA
The vibrations of the eardrum are transmitted into fluid inside a coiled structure called the cochlea.

SENSORY HAIRS
The vibrations in the fluid are detected by tiny hairs, which trigger nerve signals to the brain.

LOWER PITCH
The internal vibrations make our voices sound lower inside our own heads.

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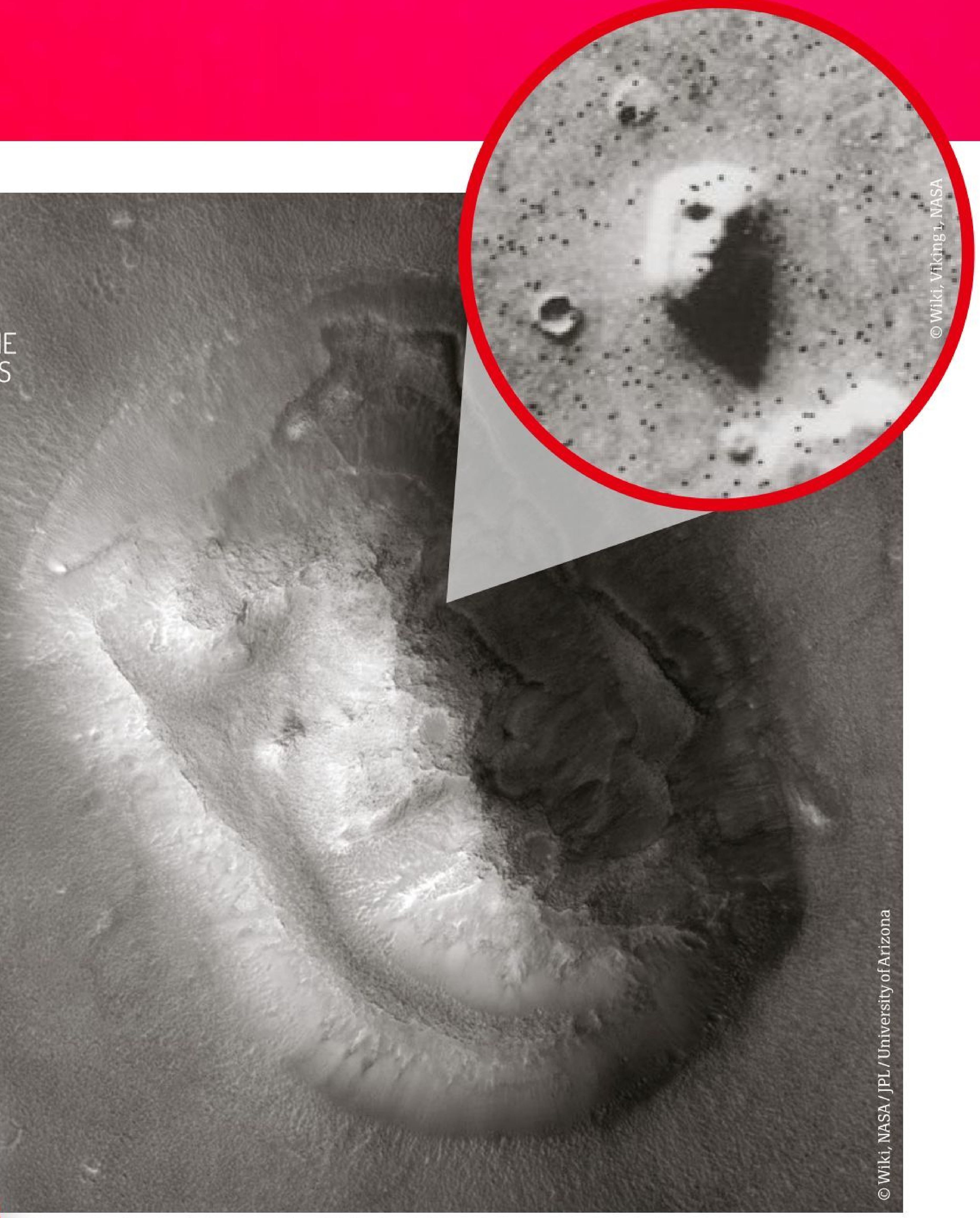
WHY DO WE SEE FACES EVERYWHERE?

From religious figures on slices of toast to aliens on Mars, faces pop up in the strangest of places. The phenomenon is known as pareidolia, and it happens thanks to a part of the brain called the fusiform face area, which is specially adapted to detect faces. If we see something that even vaguely resembles a human visage, it lights up. Researchers at the University of Toronto found that this rapid processing occurs in the prefrontal cortex (which handles what we expect to see) and the posterior visual cortex (which processes what we actually see). When people believe that they should see a face, their brain will do the rest.

SEEING FACES

YOUR BRAIN SHOULD AUTOMATICALLY SPOT THE FACES IN THESE PICTURES



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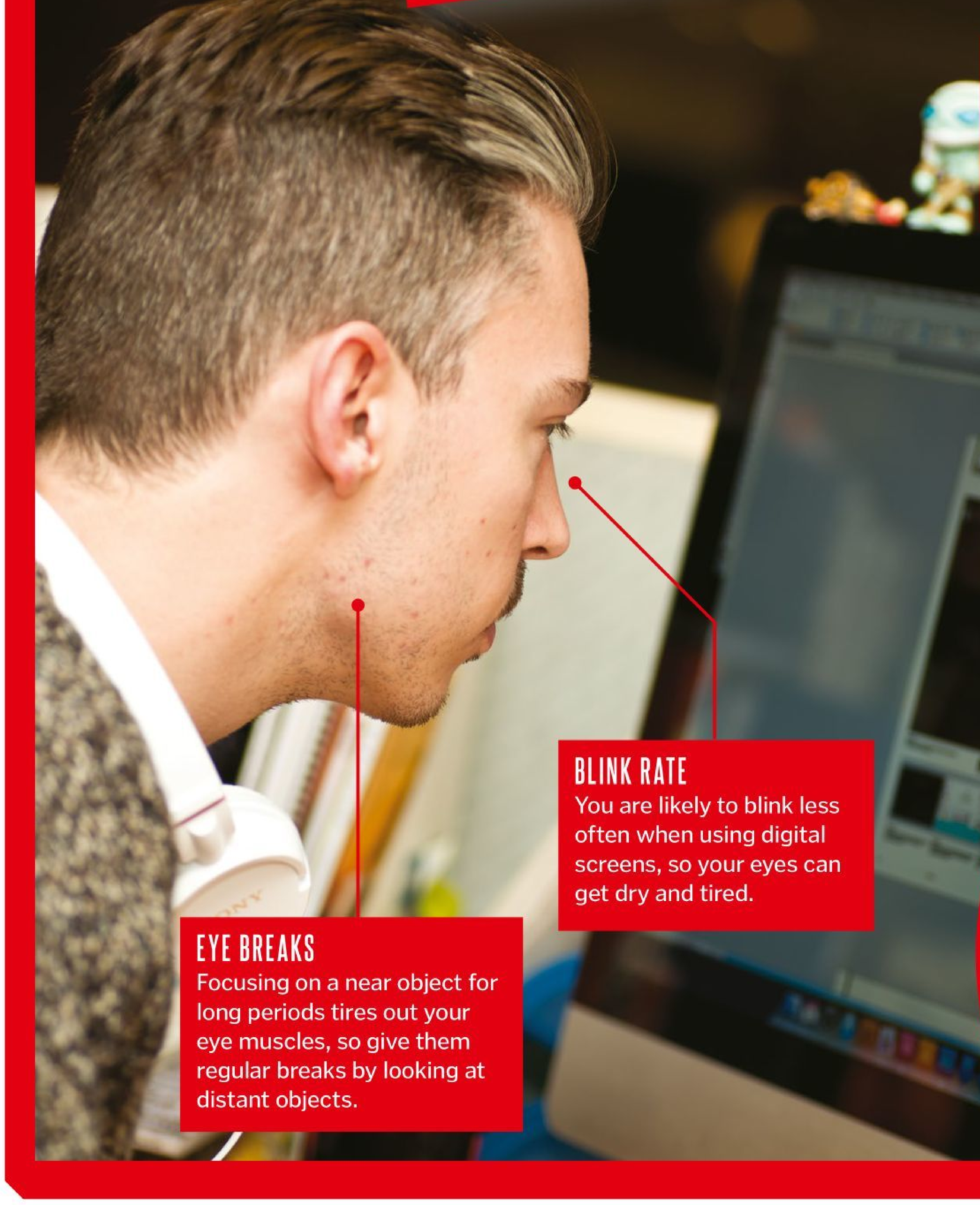


SCREEN GLARE
An anti-glare filter on your monitor can reduce the strain on your eyes.

BLINK RATE
You are likely to blink less often when using digital screens, so your eyes can get dry and tired.

EYE BREAKS
Focusing on a near object for long periods tires out your eye muscles, so give them regular breaks by looking at distant objects.

HOW DOES STARING AT A SCREEN STRAIN YOUR EYES?

The more we rely on electronic equipment for work, study and recreation, the more impact it is having on our vision. Similar to how repetitive motions can cause damage to the wrists, long periods looking at screens can temporarily strain the muscles of the eye. The lens is constantly making minute adjustments as it focuses on the screen, and glare, flicker, colour and brightness add extra layers of complexity, forcing the eye muscles to strain to keep everything looking sharp. The viewing distance and angle is often unnatural too, which can mean the eyes have to work even harder to maintain focus.

○ Repetitive motion can strain the muscles in and around your eyes

WHY DO SONGS GET STUCK IN OUR HEADS?

This irritating phenomenon has many names in the scientific literature: imagined music, involuntary musical imagery, involuntary semantic memories, intrusive songs, or slightly disconcertingly, 'earworms'.

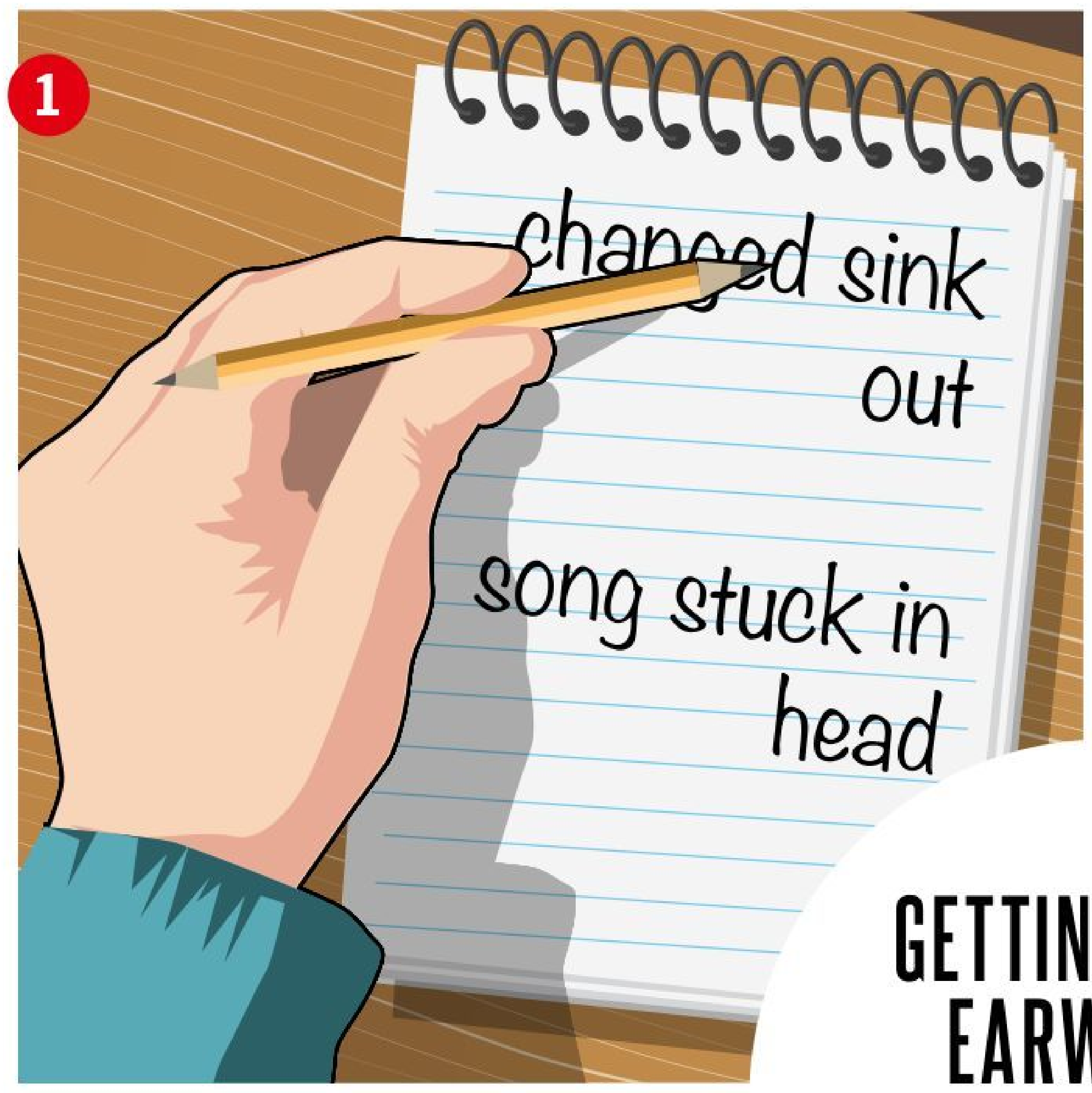
Hearing a song played on a loop inside your own brain is very common; the majority of people have experienced it, and for many it is at least a weekly occurrence. Playing music, listening to songs and singing can make it happen more often, and although people most often mention it when it becomes an irritation, it is not always unpleasant.

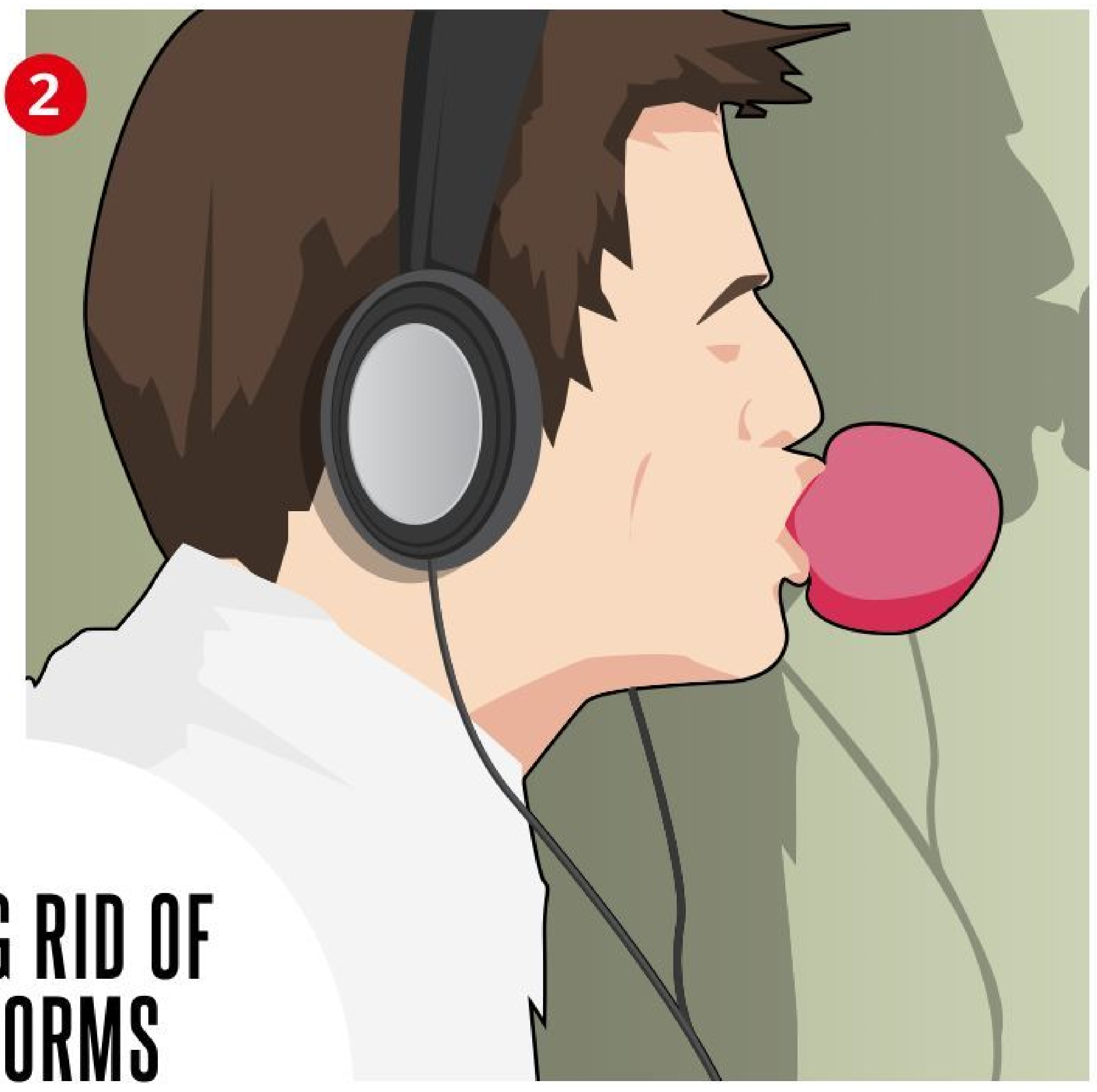
Earworms fall into the same category as spontaneous recollections of memories and mind wandering, and seem to be intrusive thoughts that are beyond our conscious control. Trying to get to the bottom of the science behind them is challenging, because researchers have to rely on the subjective reports of study participants, often through diaries and surveys that track the occurrence of earworms, and the effectiveness of different strategies to try and make them go away.

> *"HEARING A SONG PLAYED ON A LOOP INSIDE YOUR OWN BRAIN IS COMMON"*

One of the most popular ways to deal with an earworm seems to be just to leave it alone; enjoy the song, if you can, and allow the thought to pass. If that fails, distraction is another popular coping strategy, or some people even resort to engaging with the tune, listening to it in real life to get out of the loop inside their head.

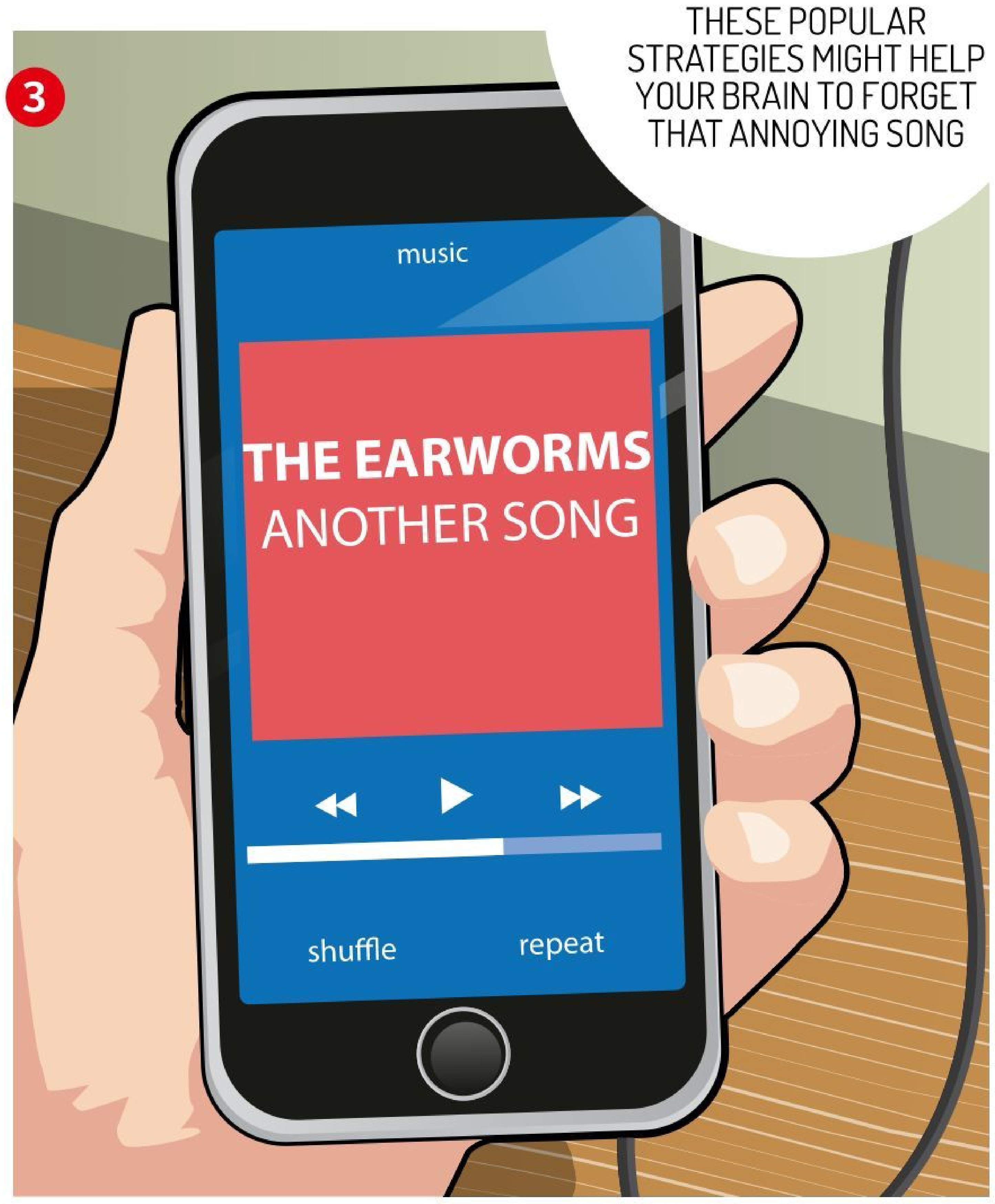
However, there is a major problem to be overcome; the more you focus on whether your attempts to get rid of the song have been successful, the more your brain is likely to go back to looping the song again. This is an idea famously explored by psychologist Daniel Wegner in his paper *Ironic Processes of Mental Control*. He points out that by monitoring whether or not you have managed to successfully get rid of a thought, you might just trigger it to start up again.





GETTING RID OF EARWORMS

THESE POPULAR STRATEGIES MIGHT HELP YOUR BRAIN TO FORGET THAT ANNOYING SONG

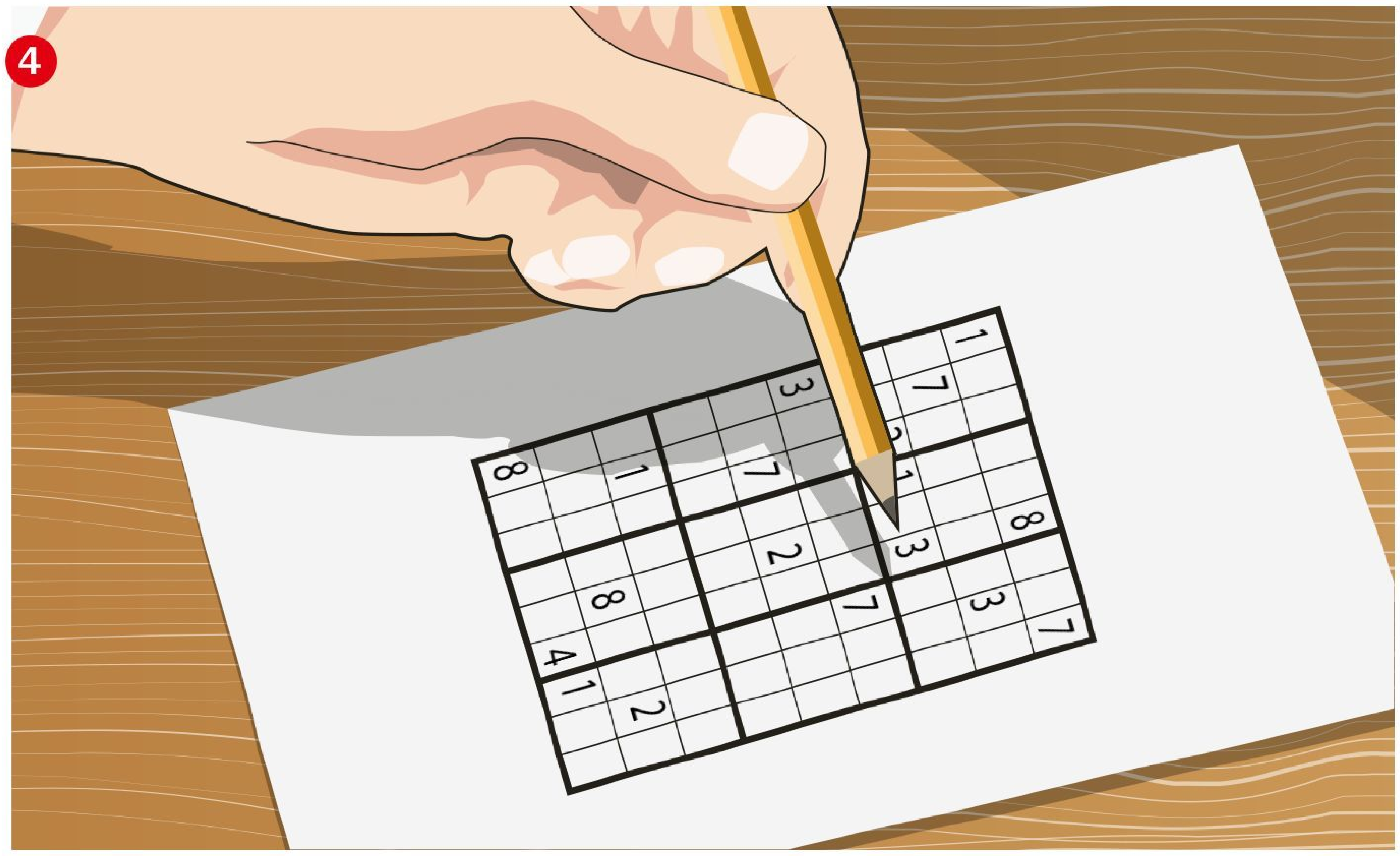


1 DOING AN ANAGRAM
Studies performed at Western Washington University showed that anagrams could provide some relief from earworms. Puzzles that aren't too challenging proved more successful than trying very complicated tasks.

2 CHEWING SOME GUM
Researchers at the University of Reading tried giving chewing gum to volunteers after they had listened to catchy songs. Movement of the jaw is thought to interfere with short-term memory and the ability to imagine sounds in your head.

3 REPLACING THE SONG
In studies performed in Finland and England, a small percentage of participants reported using 'cure' songs to relieve the frustration of an earworm; by listening to well-liked classics, they distracted themselves from the unwanted song in their head.

4 SOLVING A SUDOKU
Western Washington University researchers reasoned that performing complex non-verbal tasks could also help to keep earworms away. Easy sudokus were most effective, while challenging puzzles prompted the mind to wander.



SCIENCE INSPIRED BY NATURE

THE INCREDIBLE INNOVATIONS WE HAVE BORROWED FROM ANIMALS AND PLANTS

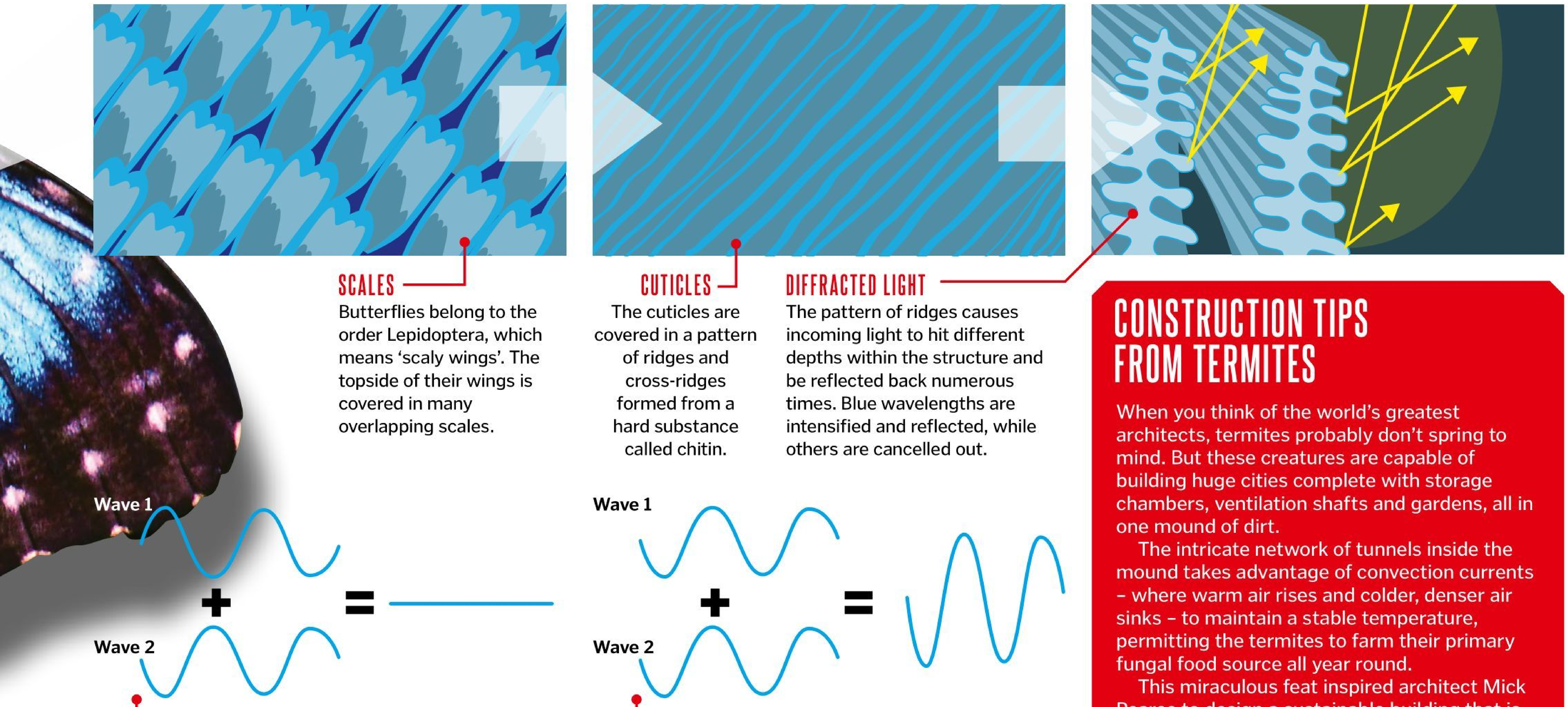
Biological organisms on Earth have spent billions of years evolving to become masters of their environments, capable of overcoming obstacles in ingenious ways to survive in a competitive world. For example, certain parasitic wasps use their long, tubular, egg-depositing organs to bore through several centimetres of solid wood, despite their inability to supply much downward force.

They achieve this by sliding the two halves of the ovipositor back and forth to penetrate further into the wood, while causing little disturbance to the surrounding area. This mechanism is quite different to drills currently used in construction and neurosurgery, but scientists have taken inspiration from this natural technique to design innovative tools, such as new steerable medical probes.

Resourceful methods such as this are abundant in the natural world, and engineers in many fields have begun to appreciate the advantages that mimicking plants and animals can bring. From construction to combat, biomimicry is helping us to discover new ways to solve old problems and opening doors to revolutionary technologies that can push our own evolution one step further.

NATURAL COLOUR

HOW A BUTTERFLY INSPIRED A FULL-COLOUR E-READER



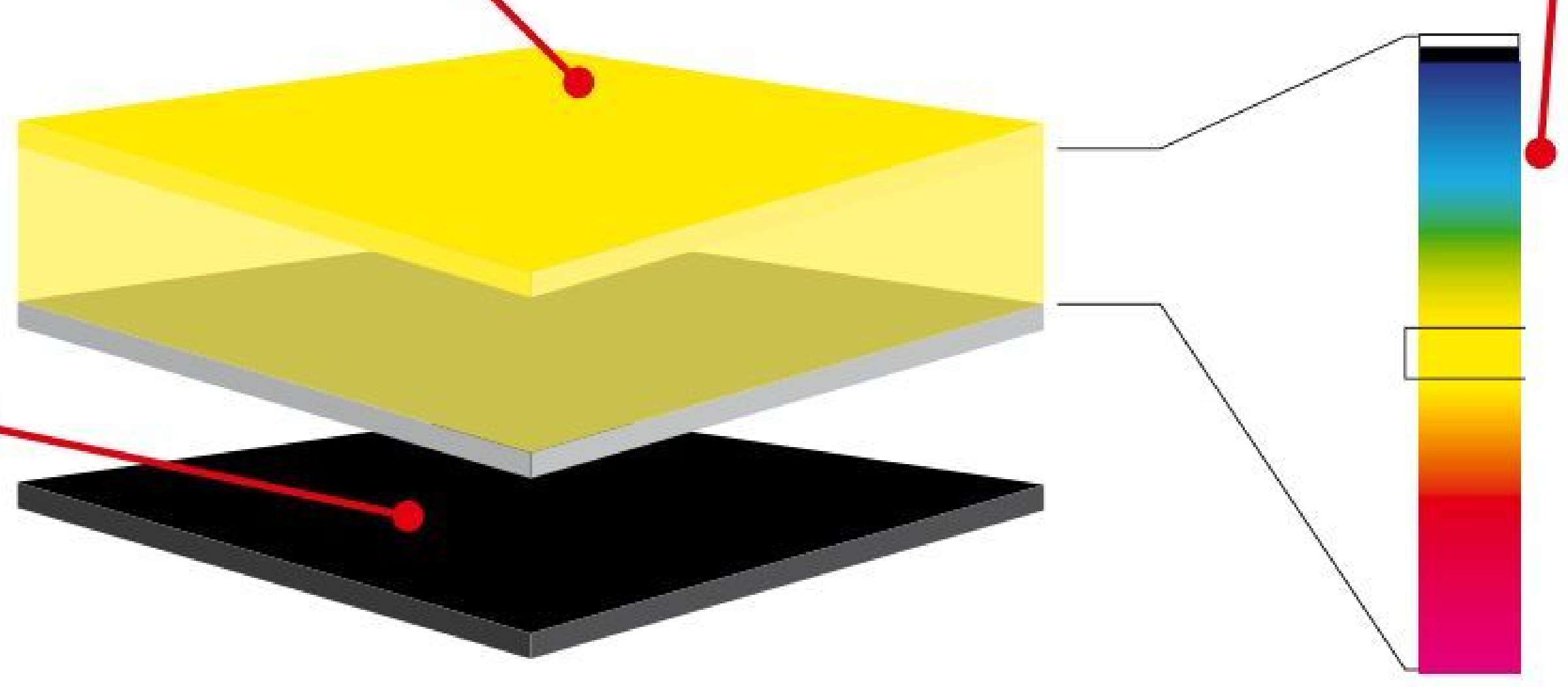
SCALES
Butterflies belong to the order Lepidoptera, which means 'scaly wings'. The topside of their wings is covered in many overlapping scales.

CUTICLES
The cuticles are covered in a pattern of ridges and cross-ridges formed from a hard substance called chitin.

DIFFRACTED LIGHT
The pattern of ridges causes incoming light to hit different depths within the structure and be reflected back numerous times. Blue wavelengths are intensified and reflected, while others are cancelled out.

DESTRUCTIVE INTERFERENCE
Wavelengths of light with conflicting peaks and troughs will cancel one another out.

CONSTRUCTIVE INTERFERENCE
Light waves where peaks and troughs align result in an amplified wavelength of colour.



PROJECTED LIGHT
External light penetrates through the glass, and wavelengths able to escape again are projected, determining the colour.

ADJUSTABLE PANELS
The size of the gaps between the panels can be adjusted, allowing only the wavelengths that directly match the size of the gap to be reflected.

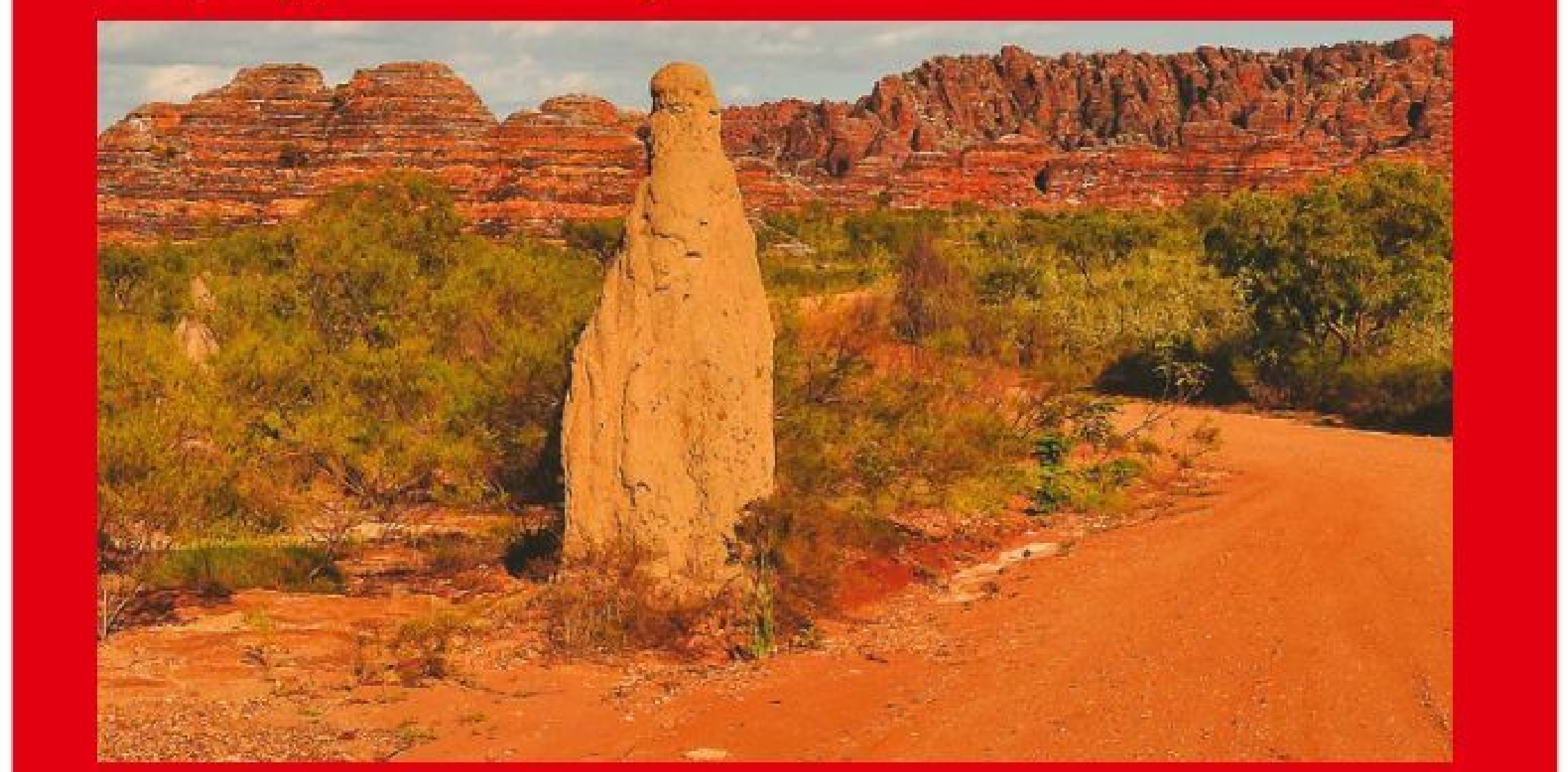
A MULTITUDE OF COLOURS
The plate gaps can be altered 1,000 times a second, allowing combinations of colours to be reflected. This enables the screen to display any colour across the visible spectrum.

CONSTRUCTION TIPS FROM TERMITES

When you think of the world's greatest architects, termites probably don't spring to mind. But these creatures are capable of building huge cities complete with storage chambers, ventilation shafts and gardens, all in one mound of dirt.

The intricate network of tunnels inside the mound takes advantage of convection currents – where warm air rises and colder, denser air sinks – to maintain a stable temperature, permitting the termites to farm their primary fungal food source all year round.

This miraculous feat inspired architect Mick Pearce to design a sustainable building that is free of air-conditioning and heating units, yet remains a comfortable temperature year-round. Using the principles of the termites, the building incorporated a series of ducts and chimneys that carried heat upwards and outwards, keeping the building cool and well ventilated.



○ Termites build complex structures to maintain stable temperatures in varying external heat

INSPIRING ANIMALS

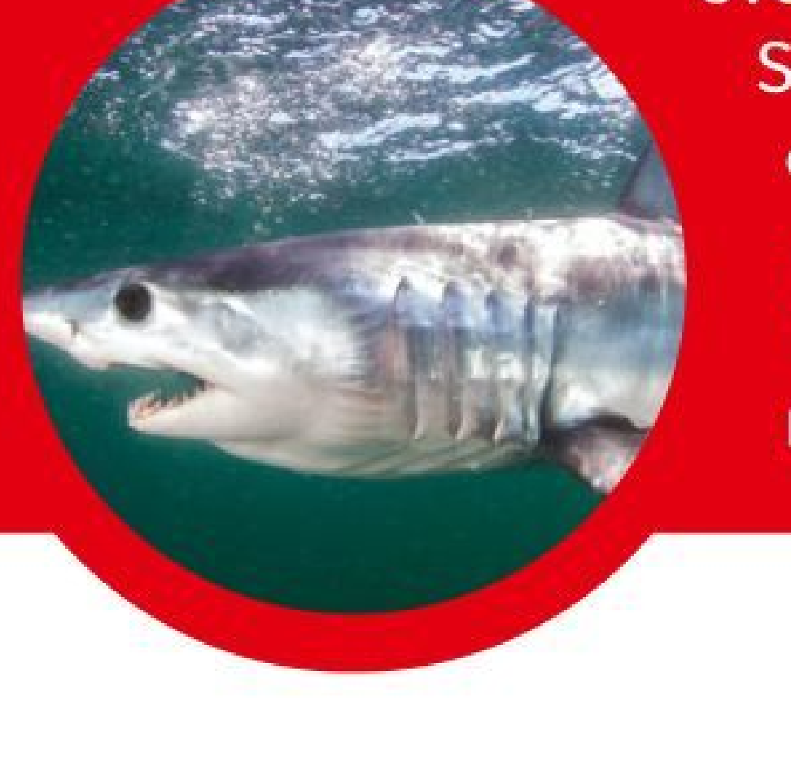
OTHER TECH AND ENGINEERING FEATS INSPIRED BY ANIMALS

IMPROVING HIGH-SPEED RAIL

Japan's 500-series Shinkansen bullet trains could travel at up to 300 kilometres per hour but created a 'tunnel boom'. Taking inspiration from the streamlined kingfisher beak, the nose was re-engineered, so newer models are quieter, faster and energy efficient.

REDUCING DRAG

Sharks are powerful predators, partly thanks to their incredible speed – some can swim at over 50 kilometres per hour! Scientists believe the bony scales covering their skin reduce drag as they move through water and have used this idea to create more hydrodynamic boats.



CAMOUFLAGED CLOTHING

Cephalopods are able to change the appearance of their skin to hide from predators or stalk prey. They use muscle contractions to expose varying pigments of colour to match their background. This has been mimicked by engineers and could be used in 'smart clothing'.

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ARTIFICIAL PHOTOSYNTHESIS

CONVERTING HARMFUL GASES INTO ECO-FRIENDLY FUEL WITH A HUMAN-MADE LEAF

Plants have been sustaining animal life for hundreds of millions of years. By absorbing carbon dioxide, water and energy from the Sun, they produce oxygen and energy in the form of carbohydrates. Scientists have now developed an artificial leaf capable of doing the same. In fact, the artificial leaf is up to ten times more efficient at capturing solar energy than its natural counterparts. It uses catalysts to split water into oxygen and hydrogen. Specialised bacteria are then able to convert the hydrogen, along with the carbon dioxide, into liquid fuels.

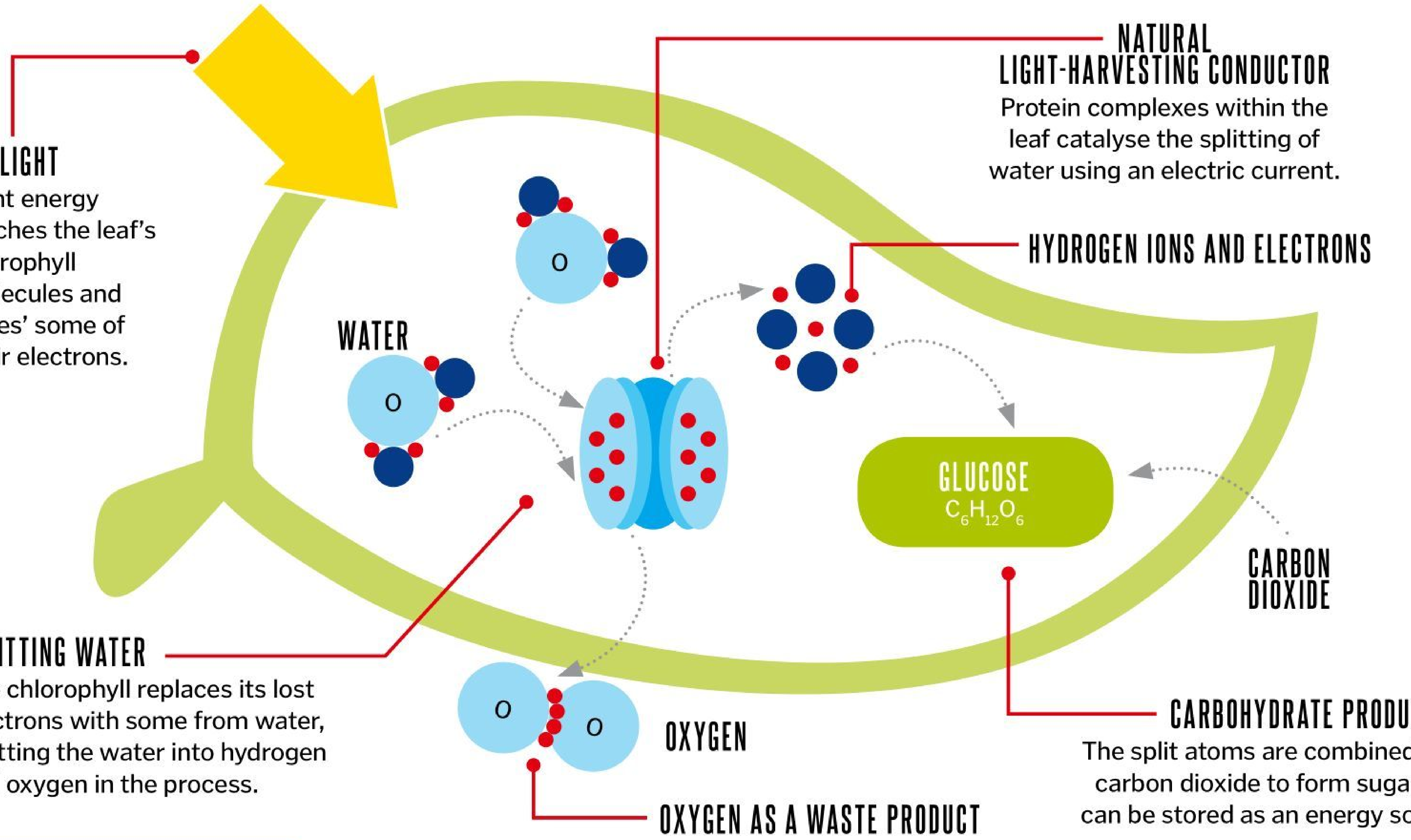
This revolutionary technology, capable of generating liquid fuel with no carbon footprint, could be an important tool in reducing our carbon dioxide emissions.

> *"The artificial leaf is up to ten times more efficient at capturing solar energy than its natural counterparts"*

HARNESSING PLANT POWER

WHETHER THEY'RE MADE IN A FOREST OR A LAB, BOTH TYPES OF LEAF OPERATE IN MUCH THE SAME WAY

NATURAL PHOTOSYNTHESIS



SUNLIGHT
Light energy reaches the leaf's chorophyll molecules and 'frees' some of their electrons.

NATURAL LIGHT-HARVESTING CONDUCTOR
Protein complexes within the leaf catalyse the splitting of water using an electric current.

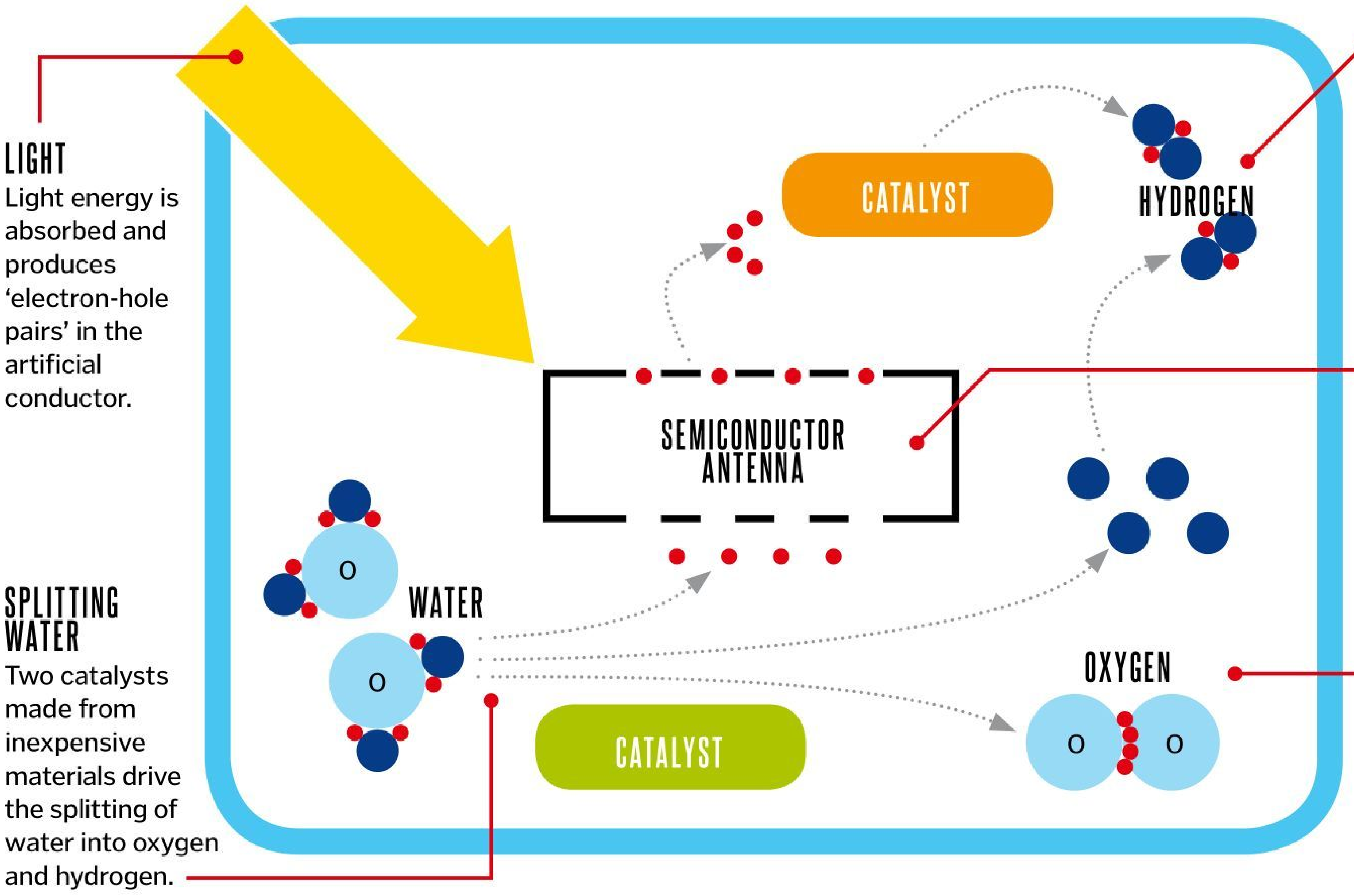
HYDROGEN IONS AND ELECTRONS

SPLITTING WATER
The chlorophyll replaces its lost electrons with some from water, splitting the water into hydrogen and oxygen in the process.

CARBOHYDRATE PRODUCTION
The split atoms are combined with carbon dioxide to form sugar that can be stored as an energy source.

OXYGEN AS A WASTE PRODUCT
The leaf releases unneeded oxygen into the atmosphere.

ARTIFICIAL PHOTOSYNTHESIS



LIGHT
Light energy is absorbed and produces 'electron-hole pairs' in the artificial conductor.

RENEWABLE ENERGY
Specialised bacteria convert hydrogen and carbon dioxide into fuel.

LIGHT-HARVESTING CONDUCTOR
Electrons from water 'jump' to the conductor, splitting the water molecules in the process.

SPLITTING WATER
Two catalysts made from inexpensive materials drive the splitting of water into oxygen and hydrogen.

OXYGEN
Like its natural counterpart, the leaf releases oxygen as a byproduct.

IMPROVING EFFICIENCY

HOW ANIMALS HAVE LED TO SCIENTIFIC DISCOVERIES

VELCRO ADHESIVES

Not having to tie your shoelaces was a great thing in the early school days, and we have biomimicry to thank for it. The invention was conceived after an engineer noticed how well the tiny hooks on plant burrs gripped to his dog's fur.

SUPERIOR WIND TURBINES

Despite their mammoth size, humpback whales are amazingly dextrous animals due to large bumps –(tubercles) found on the edges of their flippers. This feature improves lift and reduces drag as the whale performs tricky manoeuvres and could be incorporated into fans, aeroplanes and wind turbines.

HARVESTING WATER IN THE DESERT

The Namib Desert is one of the driest habitats in the world, but darkling beetles have managed to survive there by sticking their rear ends in the air and collecting water vapour. Researchers have found microscopic grooves on the beetle's forewings that help to funnel water towards their mouths. These grooves are now being incorporated into designs used for water collection devices.

MIMICKING INTELLIGENCE

AS WELL AS BEING THE SOURCE OF OUR CREATIVITY, THE STRUCTURE OF THE BRAIN IS AN INSPIRING INNOVATION

The human brain is often said to be the most complicated object in the known universe, encompassing around 86 billion neurons arranged in a massive network, where each neuron is connected to approximately 10,000 others. Our superior aptitude to learn, interpret and think creatively has helped us to cure diseases, place humans on the Moon and develop helpful computer programs that surround us in our everyday lives.

Computer power and capability has improved massively in the past few decades, and today a computer can solve a mathematical problem almost instantly, much faster than the human brain. Shops, schools, hospitals and laboratories all use these machines as an integral part of their working systems.

These tools are highly capable at certain tasks but cannot yet match the brain's most incredible attributes. Our sophisticated organ can interpret and process sensory data on an unparalleled scale; we can stand on the beach in the summer listening to the waves, watching the birds and feeling the heat of the Sun, and compose all of that data into a cohesive setting. We can also learn and adapt from experiences. Both attributes would be highly advantageous for a computer program to harness. An algorithm has recently been developed that is capable of analysing images from MRI scans to diagnose tumours or anomalies, and developers of artificial neural networks have also taken inspiration from the brain to produce programs that are capable of learning by practice.

These programs still have a long way to go to match the power of the world's greatest supercomputer, but by using the brain as a model we are getting closer to inventing a truly powerful artificial intelligence.

⬡ Dharmendra S Modha presents a brain-inspired supercomputer system containing 16 TrueNorth chips

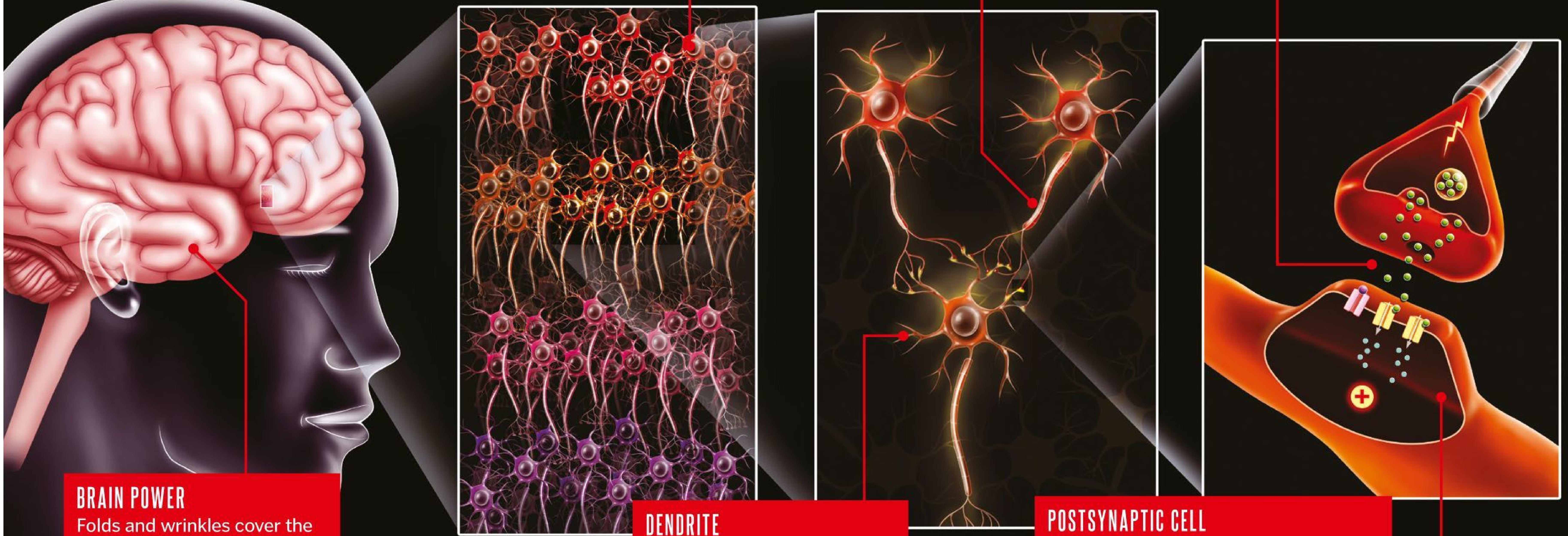
NEURONS ON A COMPUTER CHIP

Researchers at IBM have turned to the architecture of our brains to develop the TrueNorth computer chip, a brain-inspired processor with 1 million artificial neurons and 256 million artificial synapses. By mimicking the modular and flexible design of the brain, the researchers developed a scaled-down neurosynaptic network with integrated computation and memory and considerable processing power. The programming language unique to this machine is in the process of being made commercially available, so we may have brain-like computers controlling our smartphones in the near future.

> *"We may have brain-like computers controlling our smartphones"*

THE HUMAN BRAIN

OUR BRAINS ARE IMMENSE NETWORKS OF NERVE CELLS THAT FIRE ELECTRICAL SIGNALS TO EXCHANGE INFORMATION



NEURAL NETWORK
The neurons interact by transmitting electrical currents and can receive information from multiple sources.

AXON
The axon carries information away from the cell body towards the synapse.

SYNAPSE
Chemical messengers known as neurotransmitters are released and traverse the gap between neurons.

BRAIN POWER
Folds and wrinkles cover the surface of the human brain, increasing the surface area to pack in more neurons.

DENDRITE
Multiple branches, known as dendrites, receive incoming signals from other nerve cells.

POSTSYNAPTIC CELL
The combination of signals from its neighbours determines whether the next neuron will continue the message.

© SPL; WIKI; Thinkstock; Hita Bambhania-Modh IBM

ROBOTIC ANIMALS

CONSTRUCTING MACHINES IN NATURE'S IMAGE

When we imagine a dystopian future, it's almost always filled with robotic assistants. We do not have to stretch our imaginations too far to think of ways that machines could help us: they could play a role in warfare, join rescue teams, or carry our shopping. Today, many scientists are dedicated to constructing machines that can fill these roles, and finding the optimal designs was easy – nature has already provided the templates.

Animals have adapted to excel in every environment on the planet. Species exist in extreme temperatures, reside on mountaintops and live in the depths of the ocean. Engineers hope to capture their natural affinity for these locations by copying their specialised features and characteristics. Imitating animal anatomy also allows us to gift robots with admirable abilities, such as incredible speed or the power of flight.

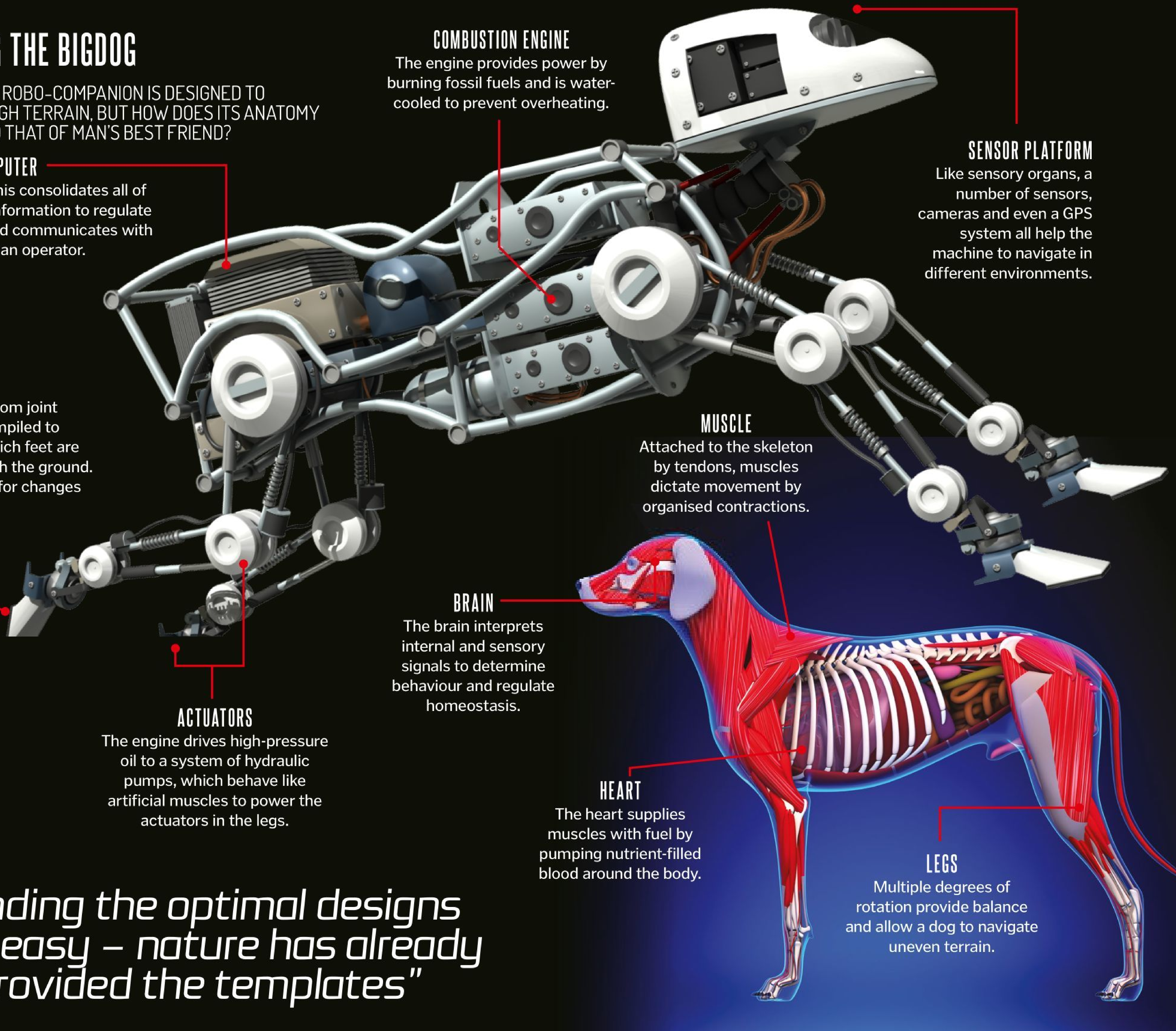
Huge inroads have already been made towards building these machines. A cheetah – the fastest land animal on Earth – reaches speeds in excess of 100 kilometres per hour thanks to its naturally flexible spine. The animal's robotic counterpart, developed by Boston Dynamics, flexes its back in a similar way to run at over 45 kilometres per hour. Meanwhile, the giant AlphaDog can carry up to 180 kilograms over large distances, the robotic equivalent of a reliable pack mule.

○ Boston Dynamics' BigDog is designed to help carry soldiers' equipment autonomously over complex terrain

From the tiny RoboBees that could pollinate crops to the ape-like android that might even help us to explore Mars, the potential applications for robot animals are endless.

BUILDING THE BIGDOG

THIS CANINE ROBO-COMPANION IS DESIGNED TO TACKLE ROUGH TERRAIN, BUT HOW DOES ITS ANATOMY COMPARE TO THAT OF MAN'S BEST FRIEND?



COMBUSTION ENGINE
The engine provides power by burning fossil fuels and is water-cooled to prevent overheating.

ONBOARD COMPUTER
Like a brain, this consolidates all of the sensory information to regulate movement and communicates with a remote human operator.

SENSOR PLATFORM
Like sensory organs, a number of sensors, cameras and even a GPS system all help the machine to navigate in different environments.

JOINT SENSOR
Information from joint sensors is compiled to determine which feet are in contact with the ground. This is useful for changes in terrain.

MUSCLE
Attached to the skeleton by tendons, muscles dictate movement by organised contractions.

BRAIN
The brain interprets internal and sensory signals to determine behaviour and regulate homeostasis.

ACTUATORS
The engine drives high-pressure oil to a system of hydraulic pumps, which behave like artificial muscles to power the actuators in the legs.

HEART
The heart supplies muscles with fuel by pumping nutrient-filled blood around the body.

LEGS
Multiple degrees of rotation provide balance and allow a dog to navigate uneven terrain.

> *"Finding the optimal designs was easy – nature has already provided the templates"*

TABBOT

A species of spider in Morocco has mastered a fancy party trick: cartwheeling. The spider, known locally as ‘tabacha’, flips up and down sand dunes to escape predators, and this athletic movement formed the blueprint for its robotic cousin, Tabbot. This machine is capable of both walking and somersaulting and has the potential to traverse deserts both at home on Earth and away on Mars.

ROBOCLAM

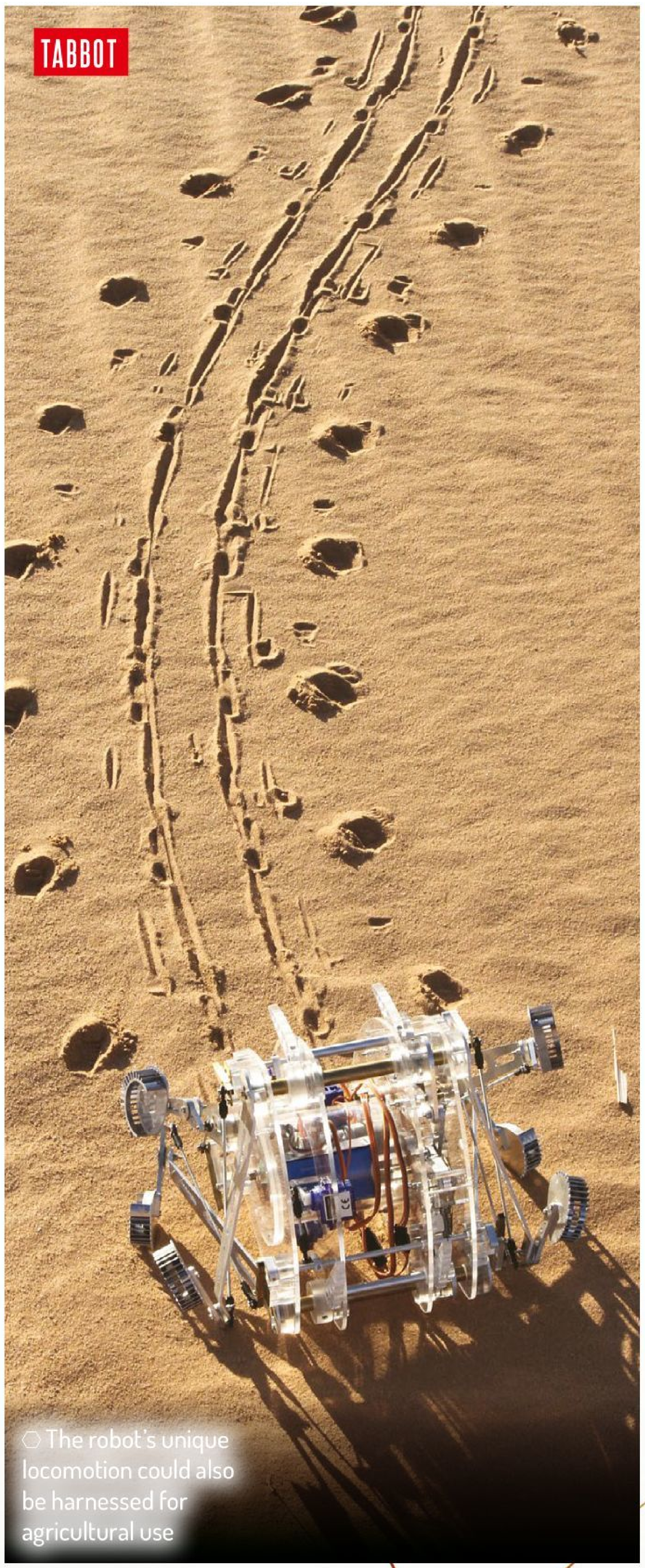
The Atlantic razor clam is a large mollusc capable of digging at incredible speeds that human drills cannot match. It achieves this by forcefully opening and closing the shells on its body to turn surrounding soil into liquid, reducing the resistance faced by the clam as it burrows further into the earth – and all at a low energy cost. Engineers have designed a mechanical device based on these principles that could be used to anchor submarines in the future.

ANTI-MINE LOBSTERS

Underwater mines pose a serious threat to military submersibles, so the US Navy has envisaged deploying robots to scout the seafloor in search of these hidden dangers. In order to develop a machine capable of effectively scouring the depths, they designed a robotic lobster – with the aim of capturing the natural version’s efficient, wave-like motion – and attached mine-detecting sensors to the frame.

RESCUE COCKROACHES

Cockroaches are typically regarded as disgusting nuisances that are notoriously difficult to kill. Researchers found their exoskeletons could withstand a force of 300 times their body weight while still moving and that they could continue to scuttle rapidly in extremely tight spaces. Their flexible design led to the inception of CRAM – or ‘compressible robot with articulated mechanisms’ – that has been constructed in the cockroach’s image. The capability of this machine to navigate through small gaps has made it an able candidate as a rescue robot, so perhaps in the future the sight of a ‘cockroach’ will bring a sigh of relief rather than a scream of terror.

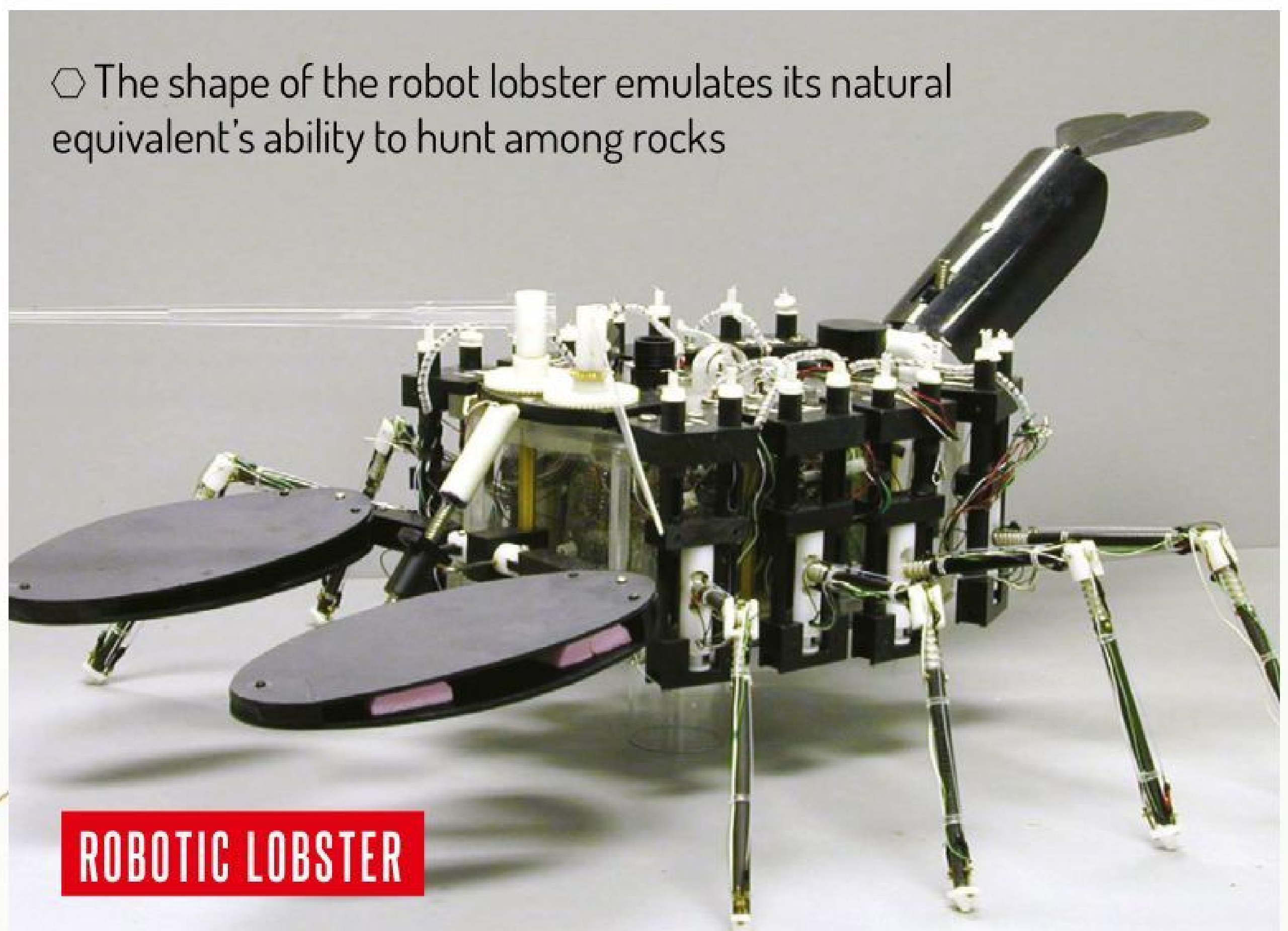

TABBOT

The robot’s unique locomotion could also be harnessed for agricultural use

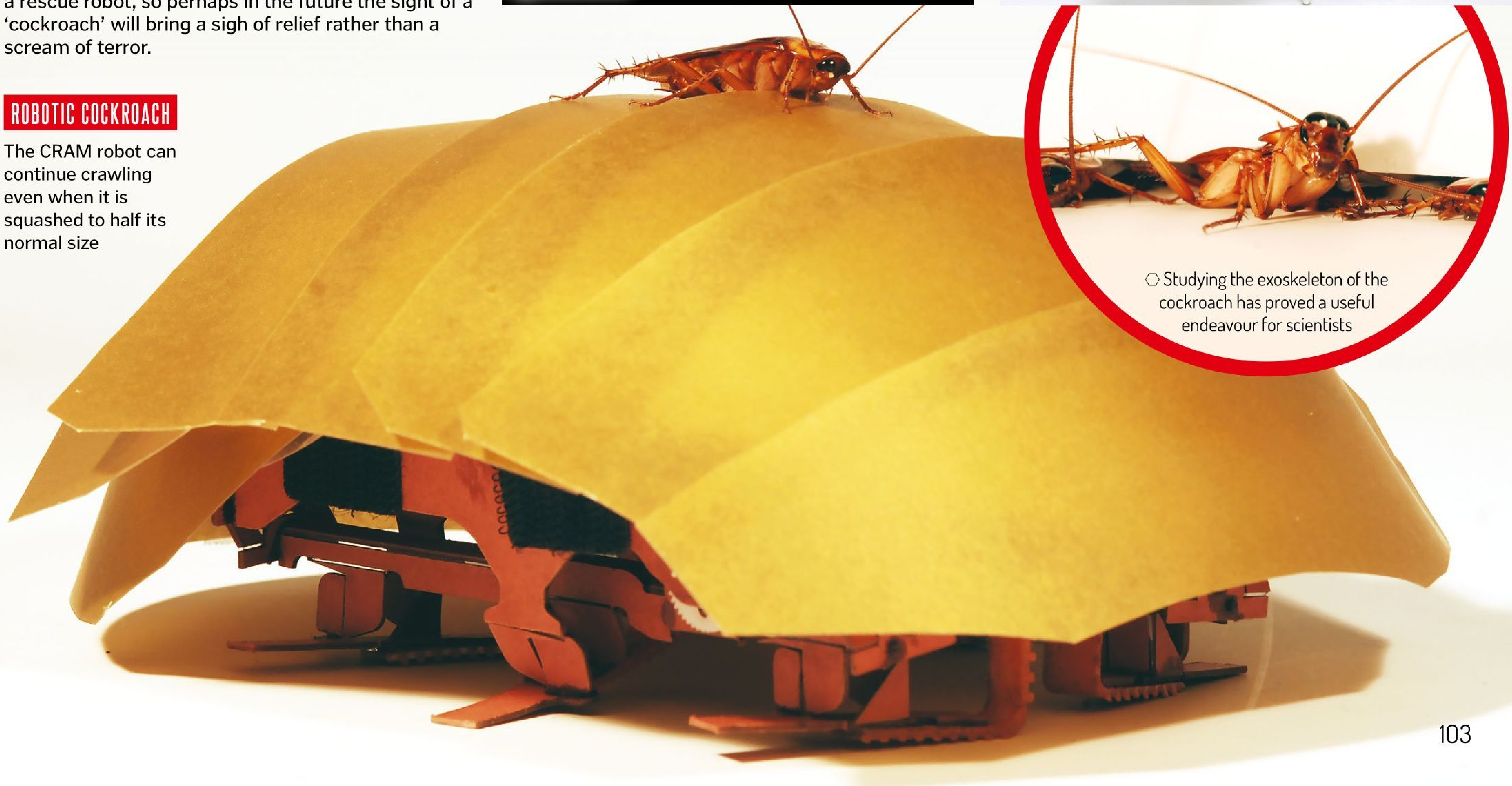
ROBOCLAM

Deep submersibles would benefit from a lightweight, reversible anchoring mechanism

> *“Perhaps the sight of a ‘cockroach’ will bring a sigh of relief”*


The shape of the robot lobster emulates its natural equivalent’s ability to hunt among rocks

ROBOTIC LOBSTER


ROBOTIC COCKROACH

The CRAM robot can continue crawling even when it is squashed to half its normal size

Studying the exoskeleton of the cockroach has proved a useful endeavour for scientists

© Tom Libby, Kaushik Jayaram and Pauline Jennings. Courtesy of PolyPEDAL Lab UC Berkeley; Thinkstock; Boston Dynamics; Donna Coveney; Illustration by Adrian Mann

ELECTROM
EXPLAINE

In 1752, as the sky darkened across Philadelphia, Benjamin Franklin went outside with a silk kite. He tied a length of wire to the top point and two strings to the bottom, one hemp and one silk. Sheltering from the storm as he worked, Franklin attached a metal key to the hemp string, now wet with rain. He kept a tight hold of the dry silk string and, as the kite struggled into the air, his experiment began.

Soaring between the lightning strikes, the wet kite started to conduct electricity from the atmosphere. Electric fire, as Franklin called it, passed down the wet hemp and into the key, sending sparks to his fingers. He gathered the charge inside a 'battery' called a Leyden jar, catching electricity from the air.

This wasn't the first time people had played with sparks. In 1663, Otto von Guericke had rubbed spheres of sulphur to produce a static charge, and in the early-18th century Stephen Gray had sent electricity coursing along hemp threads and metal wires by rubbing glass tubes. Even so, Franklin's kite was a catalyst for science that would change the world.

Spurred on by the sparking kite, experimenters set about turning observations into equations. The first mathematical explanations of electricity emerged later that century. Charles-Augustin de Coulomb realised that electrical and magnetic forces worked a bit like gravity – the closer you got to the source, the stronger they were. Later, Alessandro Volta invented a chemical battery by layering copper, zinc and brine-soaked cardboard. This allowed Georg Simon Ohm to start testing which materials could conduct a current. He used his observations to develop a law that explains how the length and diameter of a material affect its resistance to the flow of electricity.

Advances were coming thick and fast, but something was missing. No one had realised that electricity and magnetism were linked. Then, in 1820, Danish physicist Hans Christian Ørsted accidentally filled in the missing piece. He noticed that a flowing current could move the needle of a compass – it made a magnetic field. Michael Faraday then observed the reverse – a moving magnetic field made electrical currents flow.

Armed with these facts, James Clerk Maxwell went on to explain electromagnetism to the world, paving the way for the electronic revolution.

"Spurred on by the sparking kite, experimenters set about turning observations into equations"

AGNETISM

D

WHEN SCIENTISTS STARTED PLAYING WITH 'ELECTRIC FIRE' IT CHANGED THE WORLD FOREVER

THE FATHER OF ELECTROMAGNETISM

James Clerk Maxwell's four equations changed the world. The first two – Gauss' Law and Gauss' Magnetism Law – explain how electricity and magnetism move. Matter can have a positive or negative electric charge, and the flow of an electric field through a surface is proportional to the charge within that surface. But there is no equivalent magnetic charge. Magnets always have both a north and a south pole, so the flow of a magnetic field through a surface is zero. The third and fourth equations explain how electricity and magnetism interact. Faraday's Law states that a changing magnetic field induces a current, while Ampere's Law states that a flowing electric current creates a magnetic field. All four together describe how electricity and magnetism work.

○ James Clerk Maxwell unified the fields of electricity and magnetism

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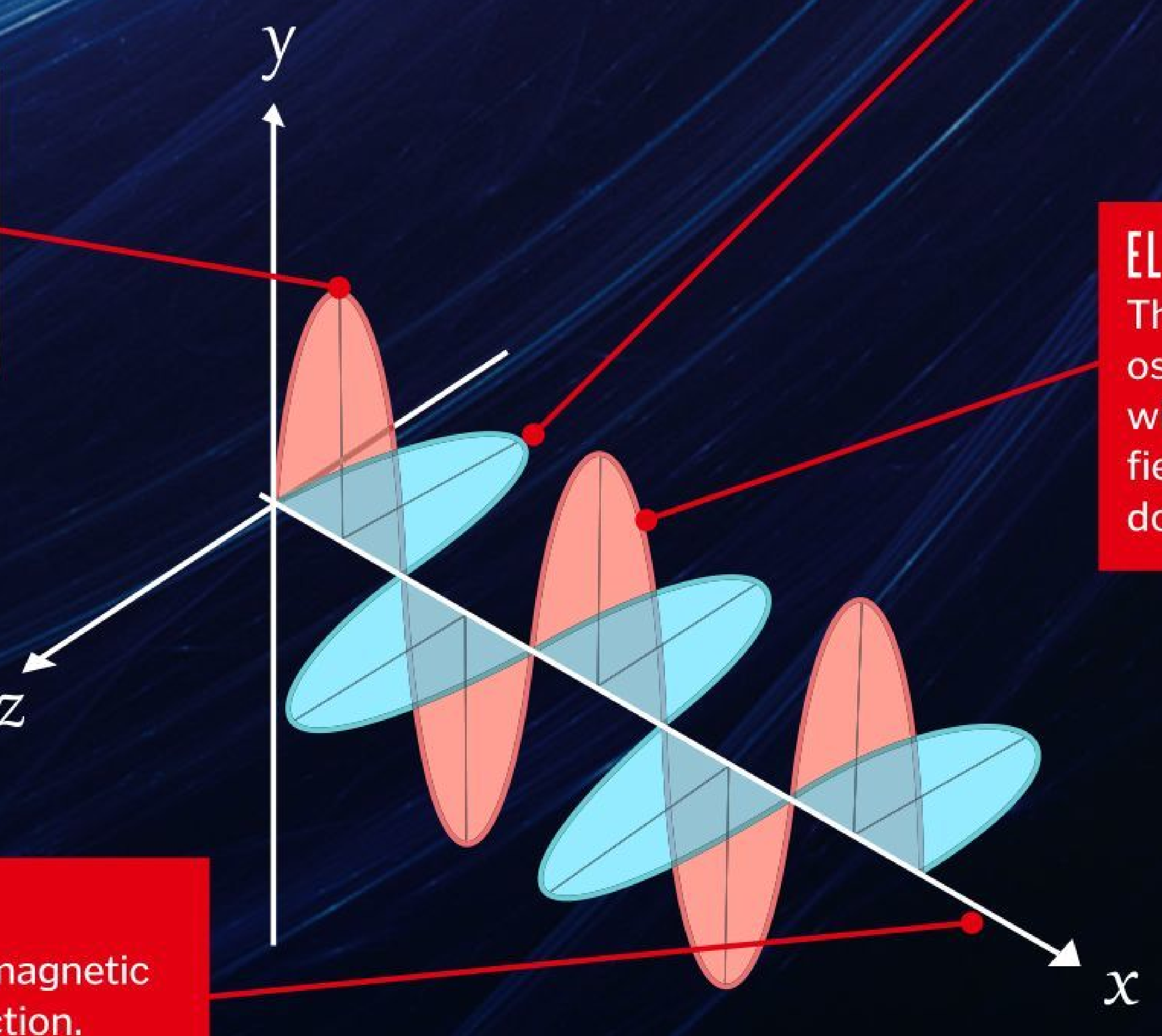
ANATOMY OF AN ELECTROMAGNETIC WAVE

THERE ARE TWO PARTS TO EVERY WAVE – AN ELECTRIC FIELD AND A MAGNETIC FIELD



MAGNETIC FIELD
The magnetic field oscillates at 90° to the electric field – they travel at right angles.

WAVELENGTH
The distance between waves can be smaller than the width of an atom or wider than the Earth.

ELECTRIC FIELD
The electric field oscillates in phase with the magnetic field – they go up and down together.

DIRECTION OF PROPAGATION
The two parts of the electromagnetic wave travel in the same direction.

FARADAY'S LAW

IN THE EARLY-19TH CENTURY A BRITISH PHYSICIST MADE A BREAKTHROUGH

Michael Faraday discovered that magnetic fields could induce electric currents. Scientists already knew the opposite was true – electric currents produce magnetic fields. In 1820, physicist Hans Christian Ørsted had been setting up a demonstration when he accidentally put a live wire near a compass. To his surprise, the magnetic needle moved. Soon after, André-Marie Ampère explained why.

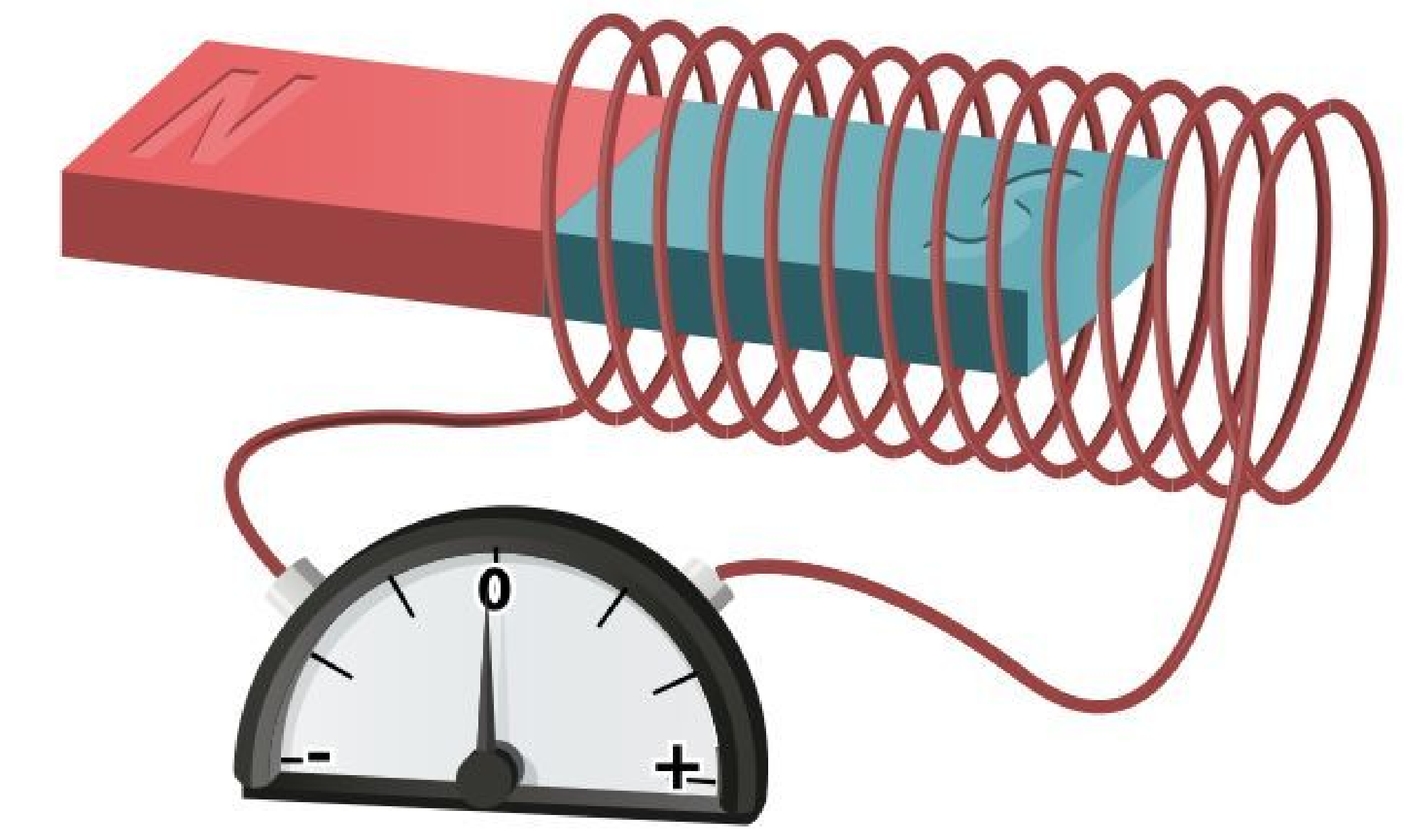
With a set of parallel wires, Ampère showed that live currents could attract and repel. When the currents ran in the same direction, the wires pulled together. When they ran in opposite directions, they pushed apart. Using these observations he worked out that the attraction between the wires was proportional to the current they carried and the length of the wires (Ampère's Law).

With Ampère's observations in hand, people realised they could amplify magnetic fields by wrapping coils of wire together. This led to the invention of the electromagnet by William Sturgeon in 1825. We could now generate powerful magnetic fields using electricity. All that remained was to show that this could happen in reverse.

To do this, Faraday wrapped two coils of wire around a ring of iron, one on each side. To the first he connected a battery, to the second a compass. The two coils were independent – the current from the battery couldn't reach the compass needle and neither could the magnetic field induced in the first wire, but, when he switched the battery on, the compass needle moved anyway. Rather than moving the compass needle directly, as in Ørsted's experiments, the magnetic field from the first wire was inducing a current in the second wire. The induced current was moving the compass. This was the first demonstration of electromagnetic induction.

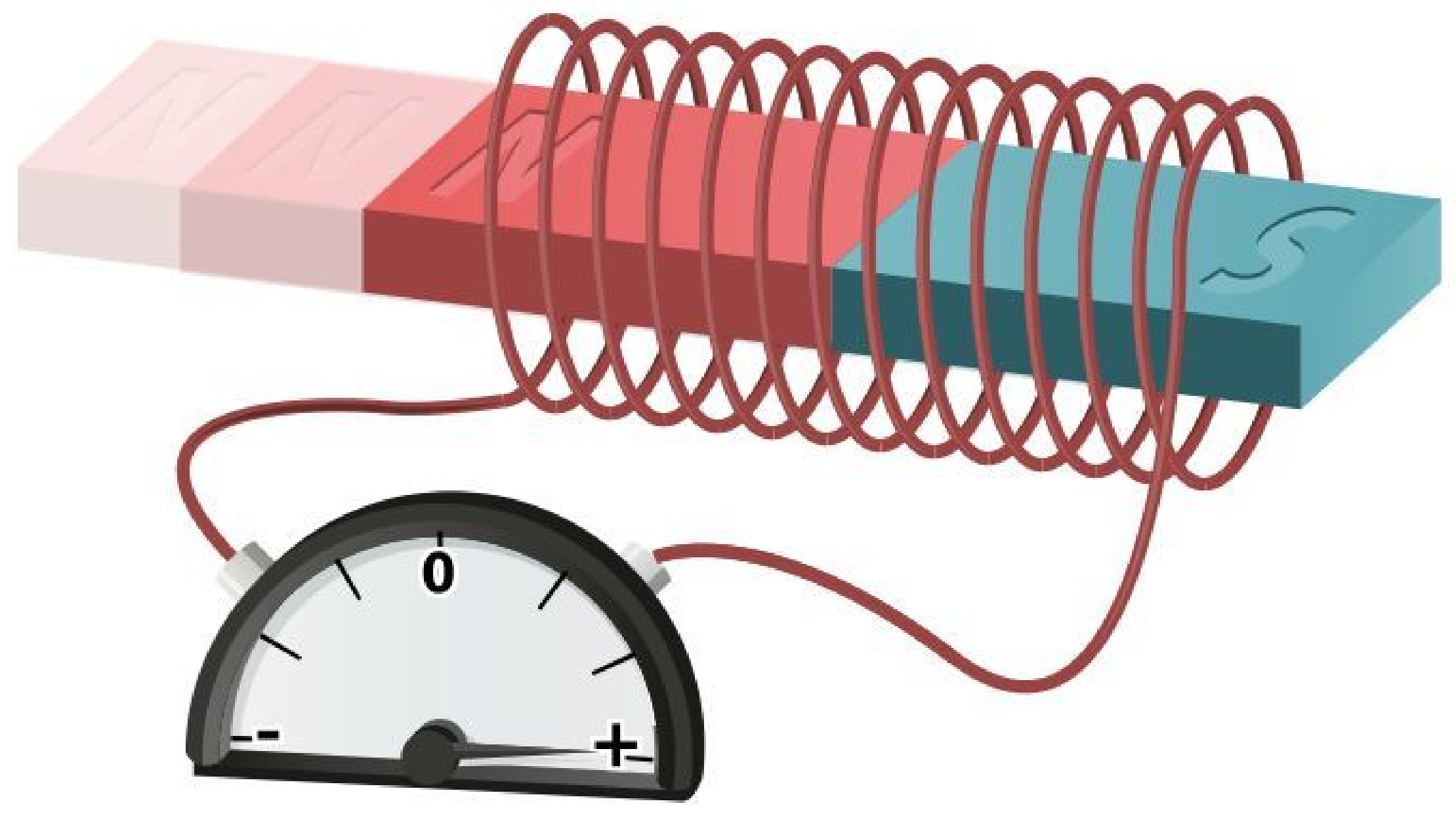
Later experiments confirmed that any changes to a magnetic field can generate a voltage. You could move or rotate a magnet inside a coil, move or rotate a coil inside a magnetic field, or vary the strength of the magnetic field itself. If the coil is part of a complete circuit the voltage sets off a current.

CREATING CURRENTS THE SCIENCE BEHIND ELECTROMAGNETISM



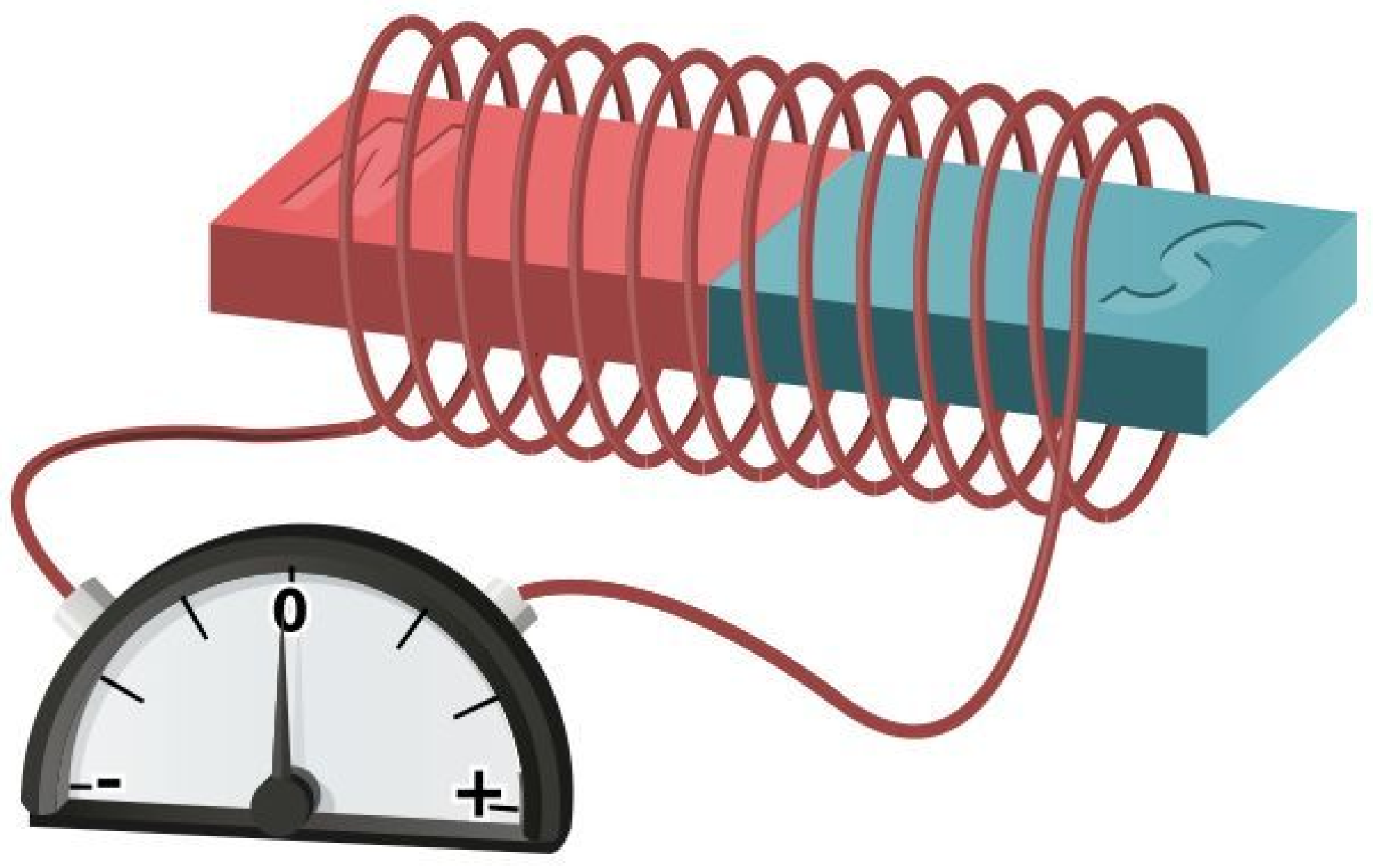
1 NO FLOW

When both the bar magnet and the coil of wire are still no current flows.



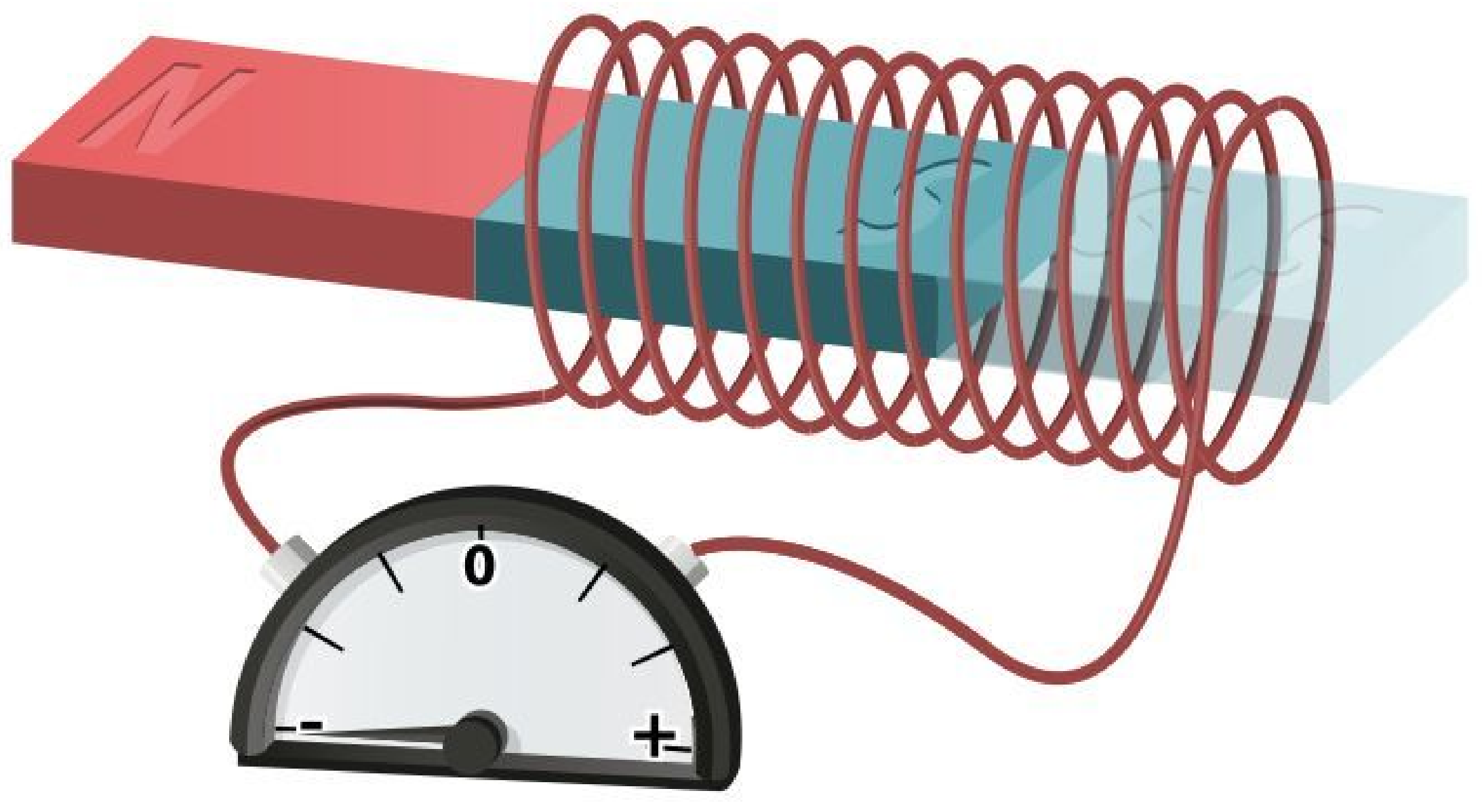
2 SPARKING TO LIFE

Pushing the magnet into the coil moves the magnetic field, inducing a current in the wire.



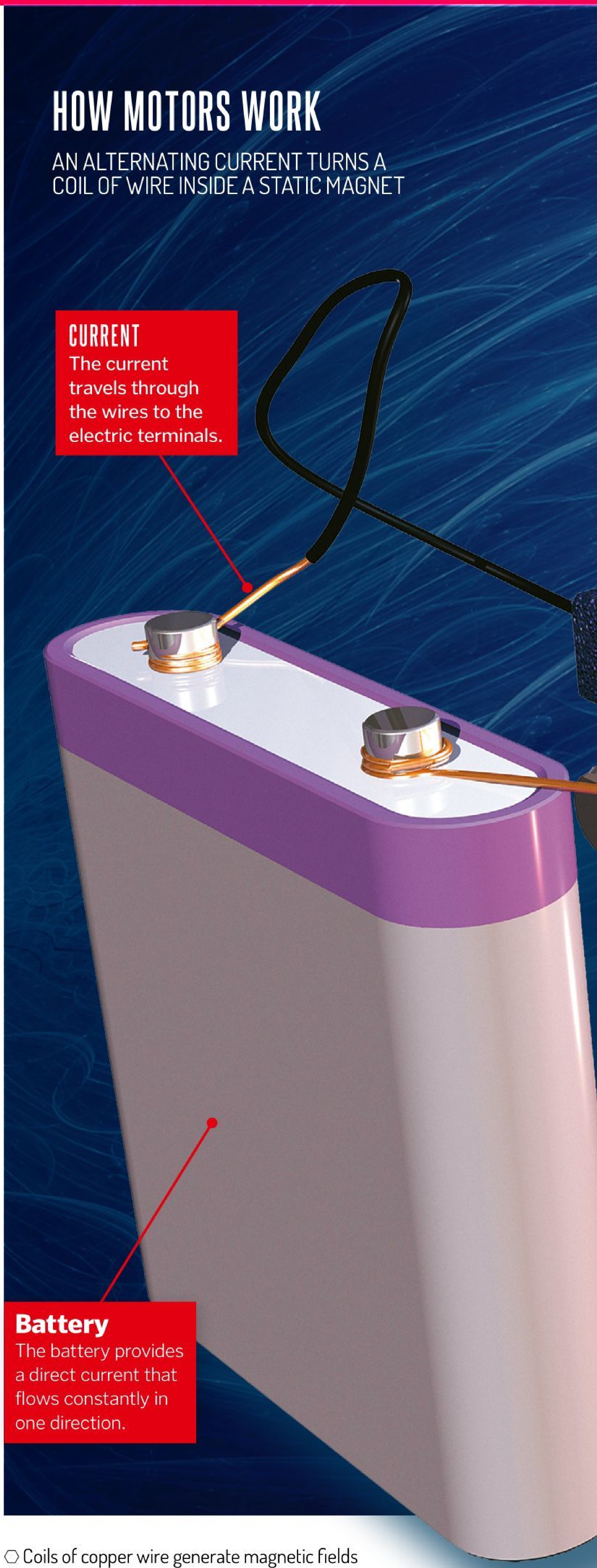
3 STOPPING THE CURRENT

When the magnet stops moving the induced current goes away again.



4 A NEW DIRECTION

Removing the magnet from the coil induces a current in the opposite direction.



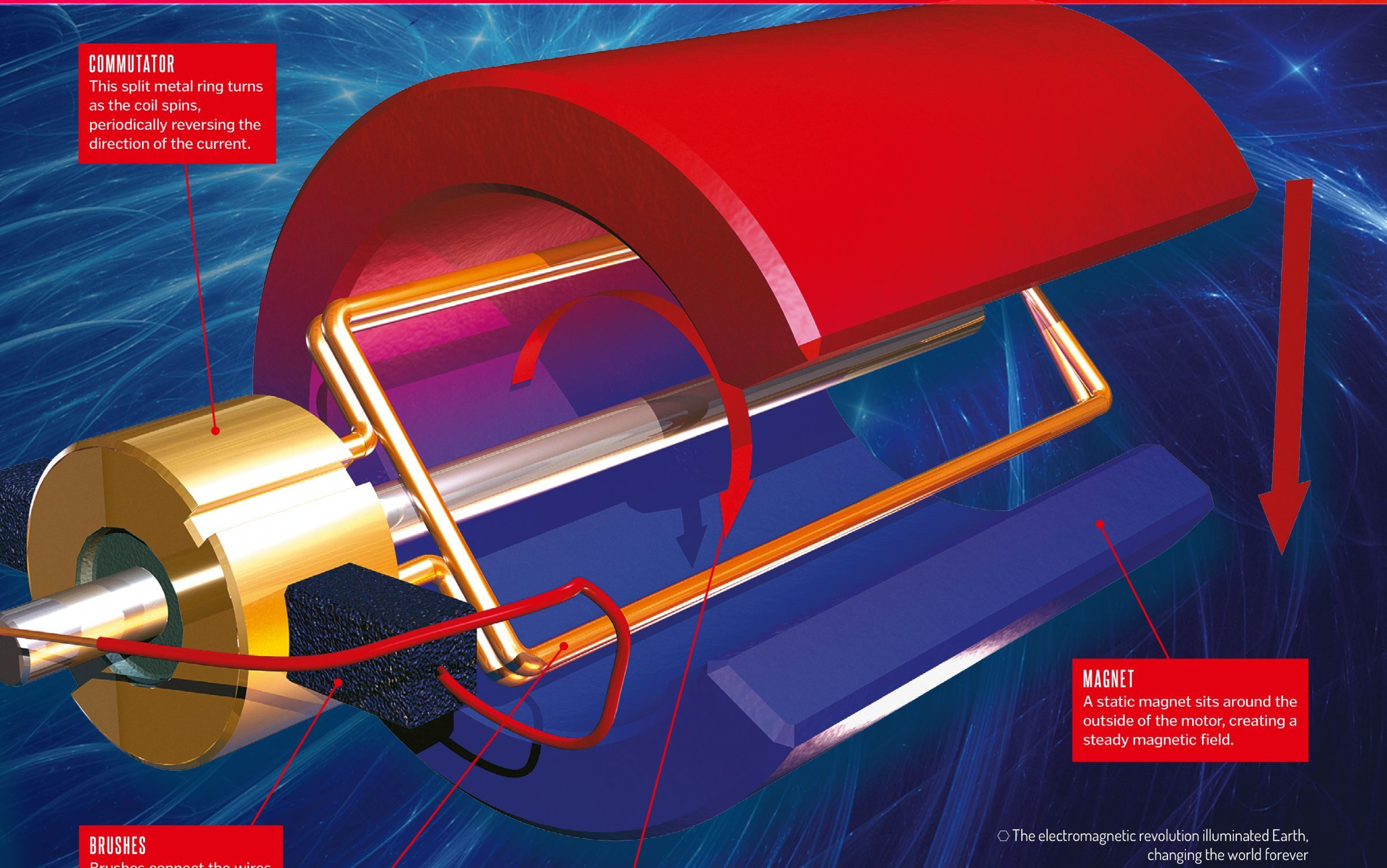
HOW MOTORS WORK

AN ALTERNATING CURRENT TURNS A COIL OF WIRE INSIDE A STATIC MAGNET

CURRENT
The current travels through the wires to the electric terminals.

Battery
The battery provides a direct current that flows constantly in one direction.

○ Coils of copper wire generate magnetic fields that make this electric motor spin



COMMUTATOR
This split metal ring turns as the coil spins, periodically reversing the direction of the current.

MAGNET
A static magnet sits around the outside of the motor, creating a steady magnetic field.

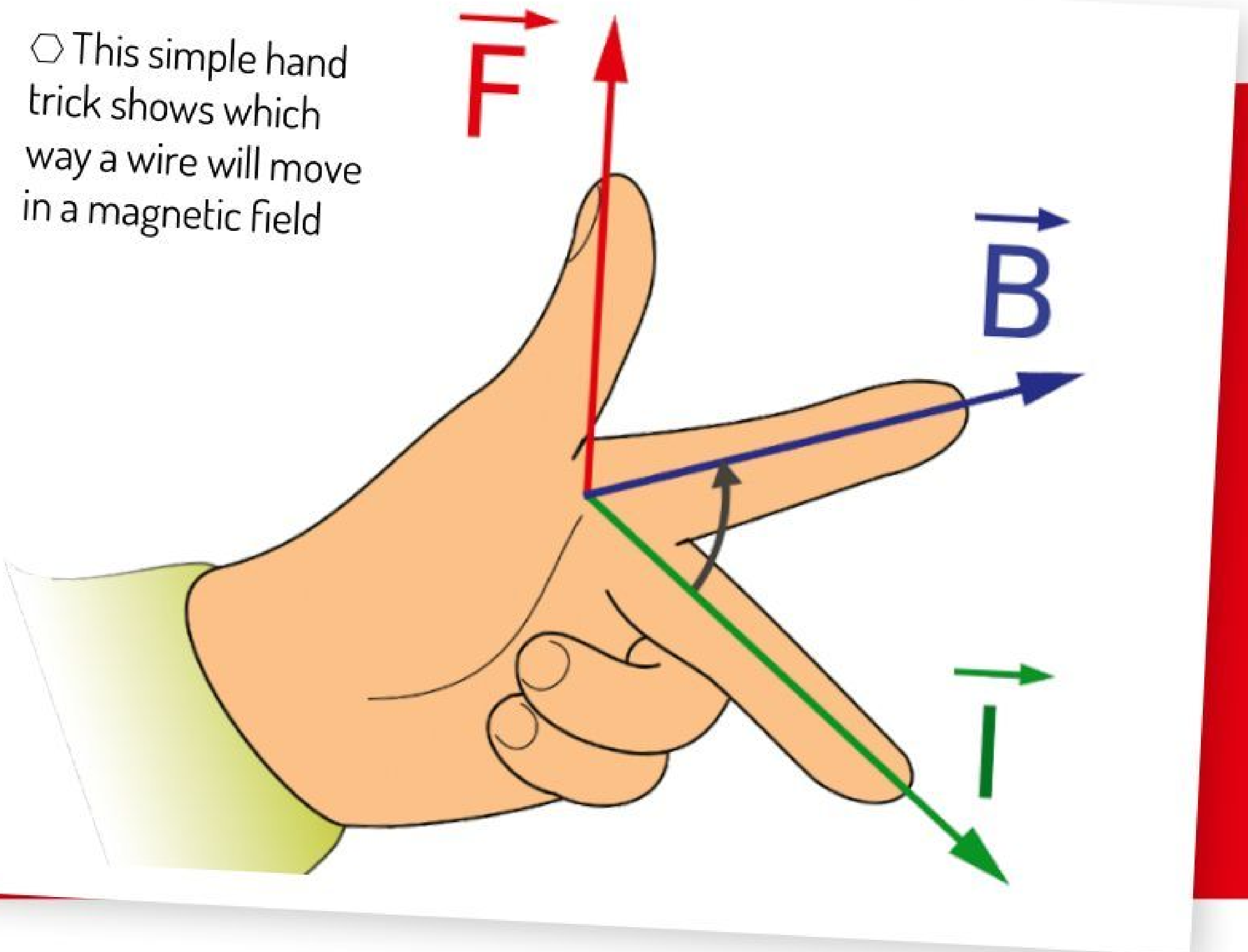
BRUSHES
Brushes connect the wires to a rotating structure called the commutator.

COIL
When a current flows through the coil it induces a magnetic field around the wire.

MAGNETIC FIELD
Changing the direction of the current flips the magnetic field induced in the coil, making it spin.

> *"People realised that they could amplify magnetic fields by wrapping coils of wire"*

○ The electromagnetic revolution illuminated Earth, changing the world forever



○ This simple hand trick shows which way a wire will move in a magnetic field

FLEMING'S LEFT-HAND RULE

When electrons move through a wire they generate a magnetic field that circles the wire like a corkscrew. Imagine applying another magnetic field across the wire. The lines of the external field try to travel from one side to the other, but they interact with the corkscrew in the middle. One field attracts or repels the other and the force makes the wire jump. Sir John Ambrose Fleming invented a rule to predict the direction of this movement. Hold out your left hand with your index finger forward, your second finger down and your thumb sticking out to the side. Point your second finger in the direction of the flowing current and your first finger in the direction of the external magnetic field. Your thumb will show you the direction that the wire will move.

© Getty; Wiki; Illustration by Ed Crooks

SEARCHING FOR INVISIBLE LIGHT

IT WASN'T UNTIL THE 1800S THAT WE STARTED TO LOOK BEYOND THE LIGHT WE CAN SEE

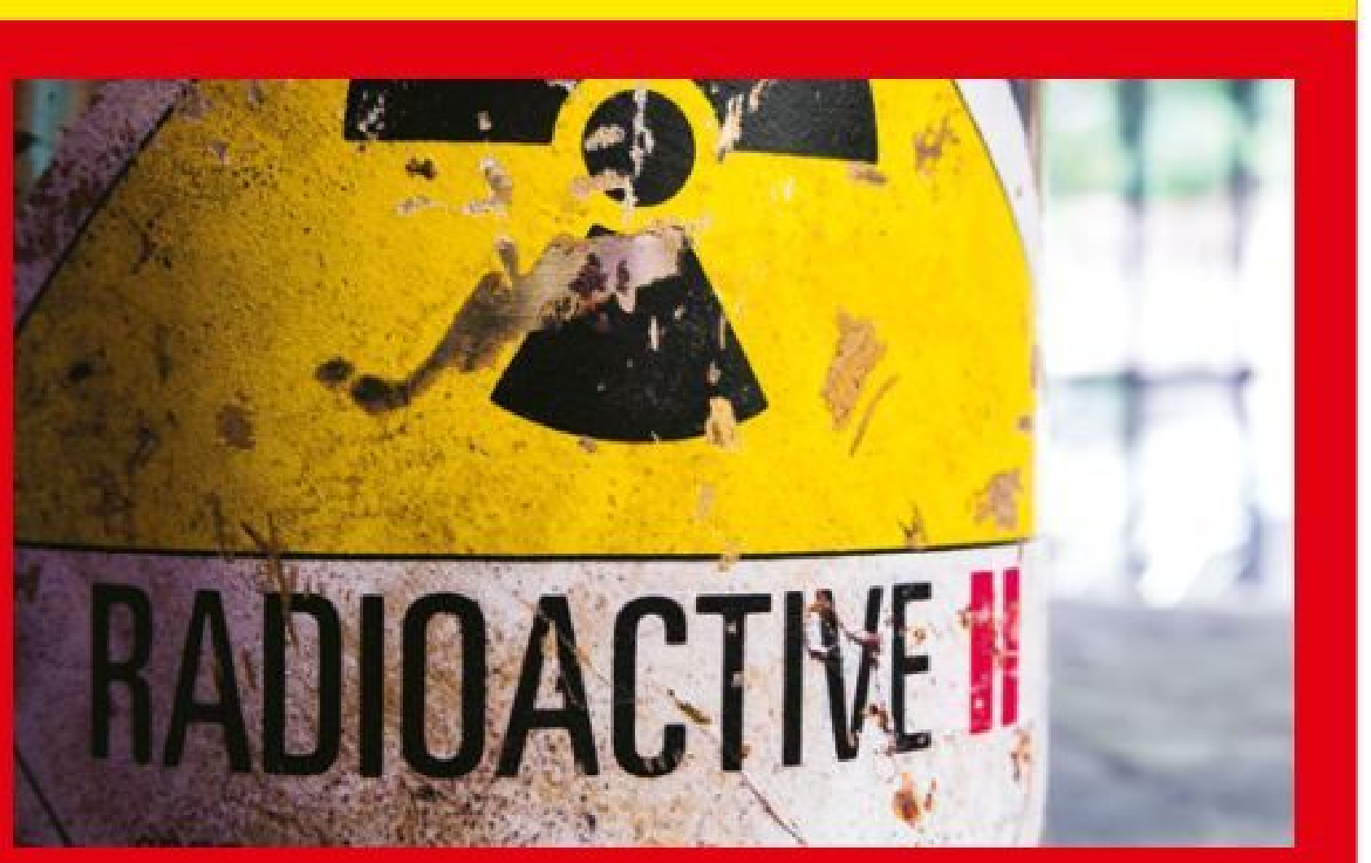
The discovery of the electromagnetic spectrum began with William Herschel, who successfully used prisms to break light into rainbows. In a bid to understand each colour's temperature he measured each ray with a thermometer and noticed something rather strange. Moving the thermometer into the darkness beyond the red edge of the rainbow increased the temperature. He'd discovered infrared light.

Fascinated by this finding, Johann Wilhelm Ritter tested the other end of the rainbow. The wavelengths at the blue end of the spectrum are cooler, so instead of using a thermometer he chose a chemical called silver chloride. He knew it turned black in light and that the effects were faster as the light became more purple, and, just as Herschel had noticed, the effect continued when the rainbow ran out. He'd discovered ultraviolet light.

Inspired by this work, James Clerk Maxwell predicted there would be more wavelengths beyond the rainbow. Heinrich Hertz designed a piece of equipment called a spark-gap transmitter to find them. He wrapped two insulated coils of wire around some iron, one loose and one tight. When a current passed through the loose coil it magnetised the iron. Then he stopped the current and the magnetic field faded, inducing a large voltage in the

GAMMA RAYS

The highest-energy electromagnetic waves are the gamma rays. Like both ultraviolet light and X-rays, they count as 'ionising radiation'. When they hit molecules they can knock electrons away, creating reactive ions that can damage cells and tissues. We can harness this power to treat certain types of cancer.



+ HARMS CANCER CELLS.
KILLS BACTERIA.

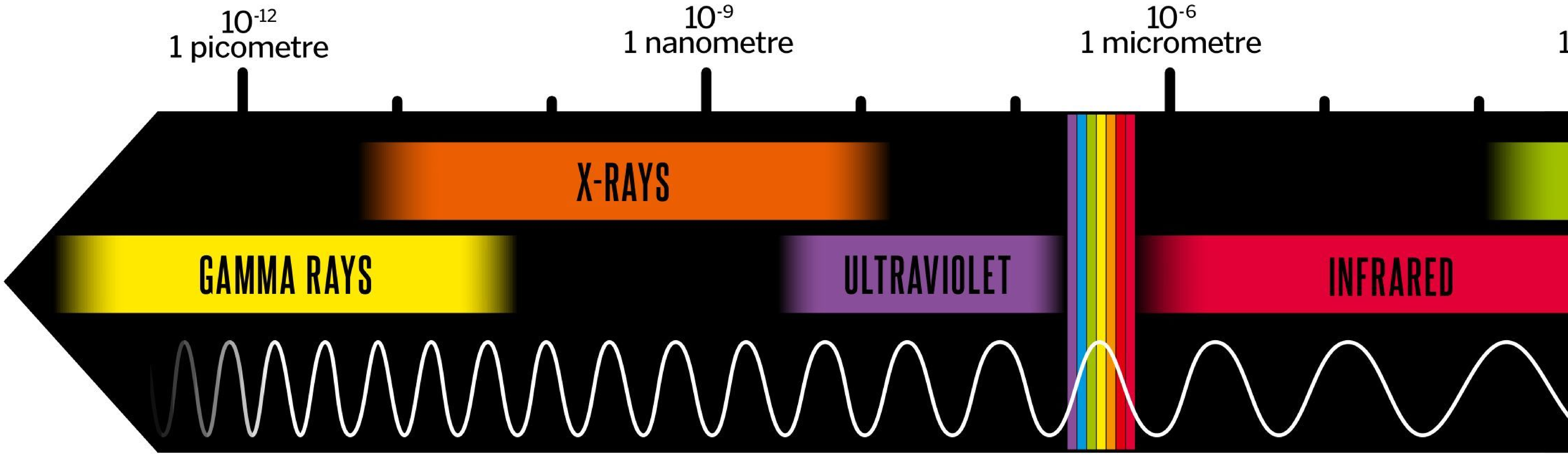
− CAUSES CANCER.
BURNS THE SKIN.

X-RAYS

X-rays are more powerful than ultraviolet light and their wavelengths are shorter. This allows them to travel through the human body rather than just into the skin. Different materials absorb different amounts of energy, revealing bone and metal on X-ray images, but prolonged exposure can cause harm.

+ TRAVELS THROUGH THE BODY.
SCANS INSIDE OBJECTS.

− CAUSES CANCER.
CAN'T SHOW FINE DETAIL.



ULTRAVIOLET LIGHT

As we move into the higher-energy part of the spectrum the radiation gets more dangerous. Ultraviolet light can damage molecules like DNA and collagen, causing sunburn, skin ageing and skin cancer. But we can also put UV light to good use – it kills bacteria and makes fluorescent materials glow.

+ KILLS BACTERIA.
EXCITES FLUORESCENT MATERIALS.

− DAMAGES THE SKIN.
CAUSES CANCER.

VISIBLE LIGHT

Not only does visible light allow us to see and make sense of the world around us, but we can also use it for long-distance communication in fibre optics. Visible light zips through glass cables across long distances, allowing lightning-fast information transfer.

+ DETECTABLE BY THE EYES.
TRAVELS THROUGH GLASS.

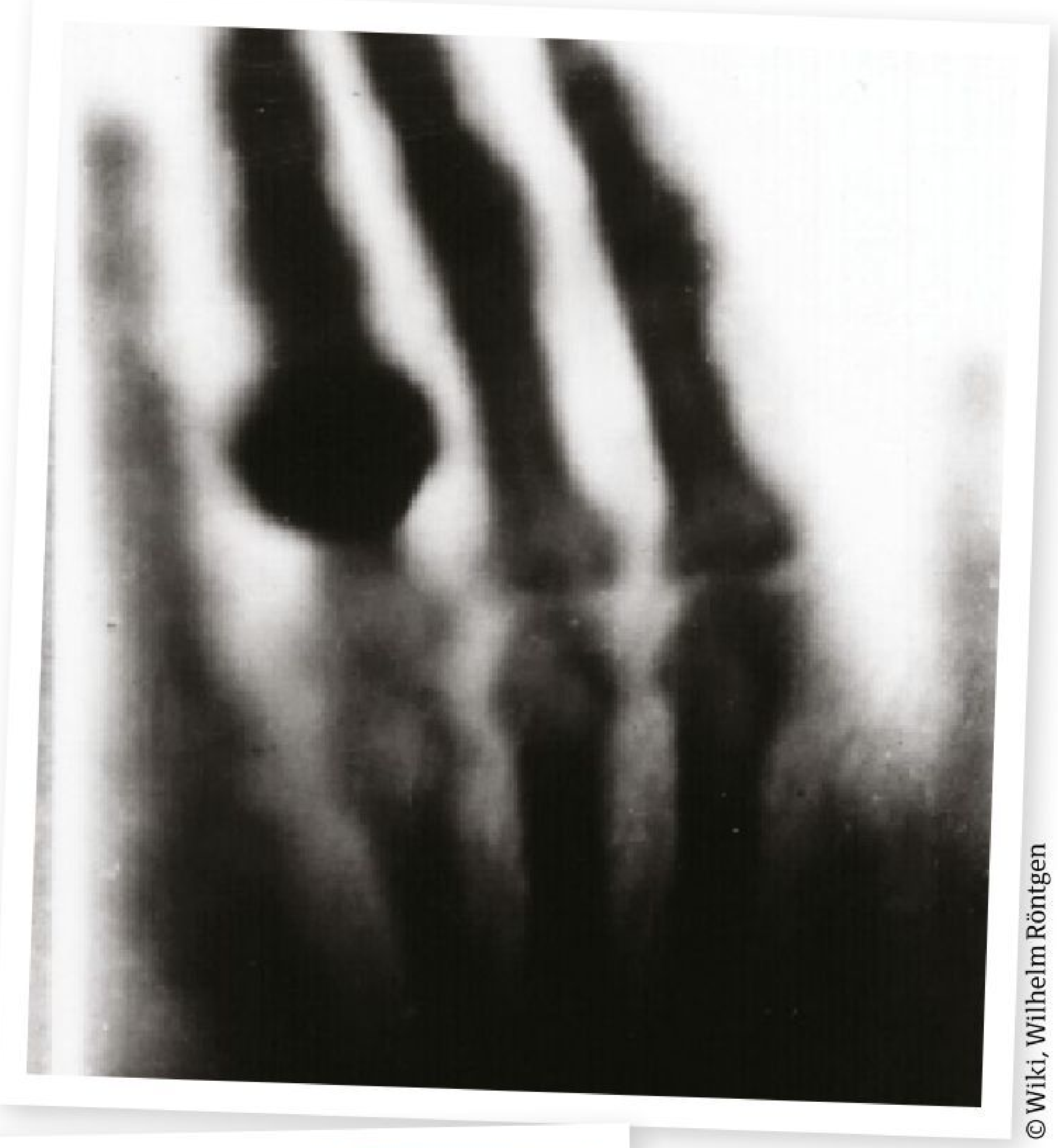
− SMALL PART OF THE SPECTRUM.
DAMAGES THE EYES.

> "When he asked his wife to put her hand between the tube and screen it created the first X-ray"

second coil. Hertz attached the second coil to copper wires separated by a small gap, and whenever the large voltage came a spark would jump from one side to the other. A metre and a half away he set up a rectangle of copper wire with another spark gap. He noticed that when the first gap sparked, the second gap sparked too – the current created radio waves that travelled across the room. Hertz also experimented with microwaves.

Wilhelm Conrad Röntgen was the next to make a breakthrough. He was experimenting with a piece of kit called a vacuum tube, which has an anode and a cathode inside an enclosed container. He happened to have a screen in his lab coated in a fluorescent chemical called barium platinocyanide. He noticed that even if he covered the vacuum tubes and worked in the dark the screen would glow when he switched the current on. When he asked his wife to put her hand between the tube and the screen it created an image of her bones – the first X-ray.

Soon after, while investigating the radiation emanating from radium, Paul Villard discovered gamma rays, completing the electromagnetic spectrum.



© Wiki, Wilhelm Röntgen

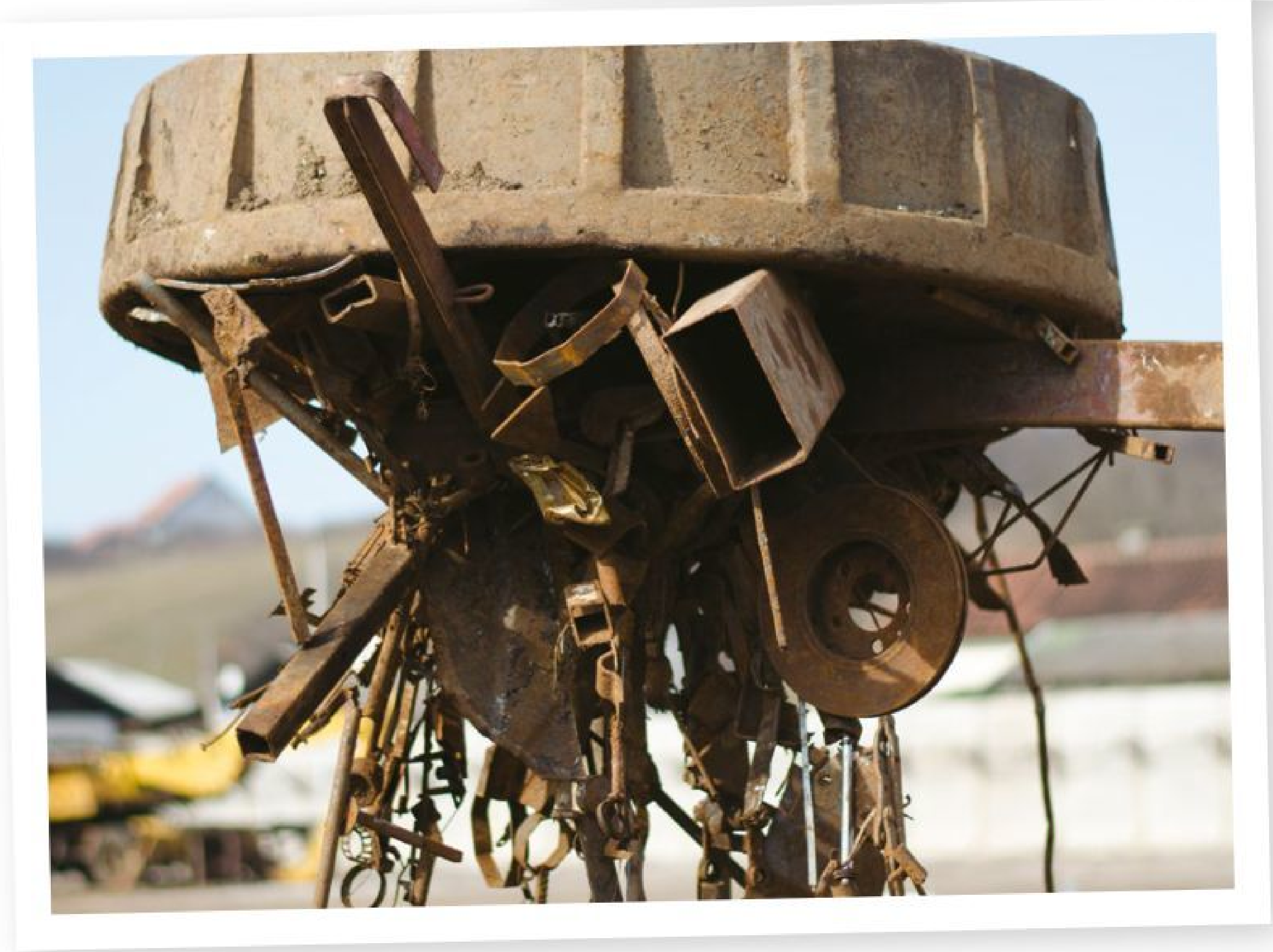
○ Wilhelm Röntgen's wife, Anna Bertha Ludwig, was the first person ever to have an X-ray

INFRARED LIGHT

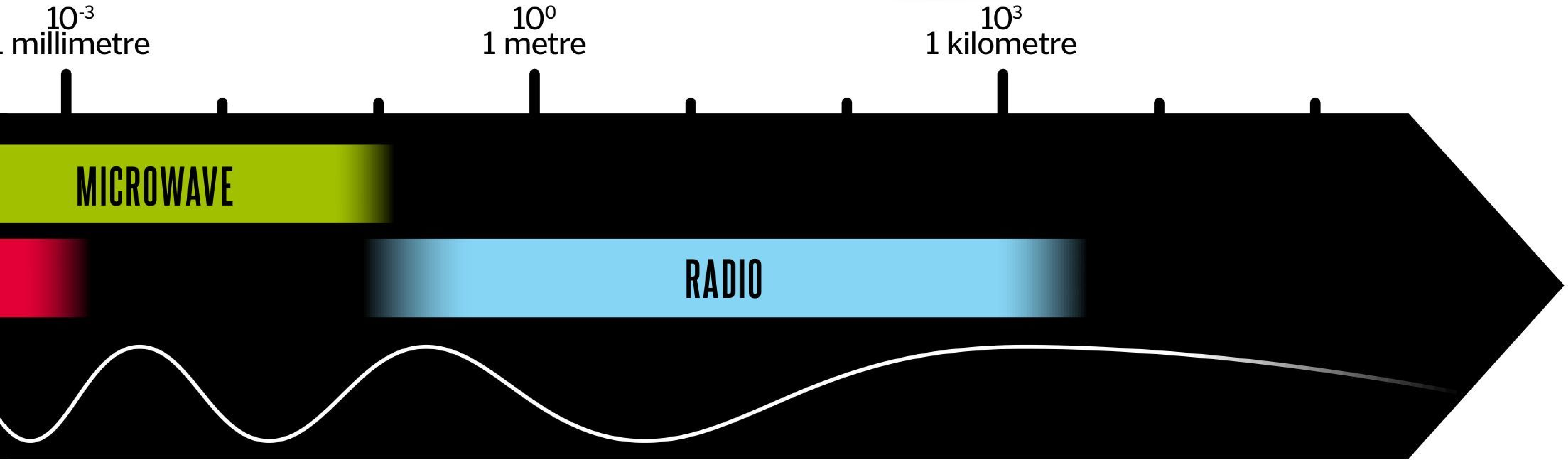
This type of radiation transmits heat across the universe. It interacts with chemical bonds, increasing their energy level and heating them up. We use it to cook our food and heat our homes and for thermal imaging. It can also transmit information over short distances, including using a television remote control to change the channel.

+ TRANSMITS HEAT.
EMITTED BY ALL OBJECTS.

− CAUSES BURNS.
ABSORBED RAPIDLY.



○ Industrial electromagnets use Ørsted's science to lift scrap metal with electricity



MICROWAVES

Like radio waves, microwaves can store and send information. We use them for mobile phone communications and to talk to satellites. They also interact with the water in food and drink, transferring energy and heating the molecules – this is the technology behind microwave ovens.

+ CARRIES DATA.
PASSES THROUGH ATMOSPHERE.

− CAUSES BURNS.
SUPERHEATS WATER.

RADIO WAVES

Radio transmitters send out signals called continuous sine waves. By changing the amplitude or frequency these sine waves can carry patterns of information through the air. When they hit an antenna they induce an electric current with the same patterns, thereby passing the message along.

+ TRAVELS LONG DISTANCES.
DOESN'T HARM THE BODY.

− LIMITED DATA STORAGE.
ATMOSPHERIC CONDITIONS CAN INTERFERE WITH SIGNAL.

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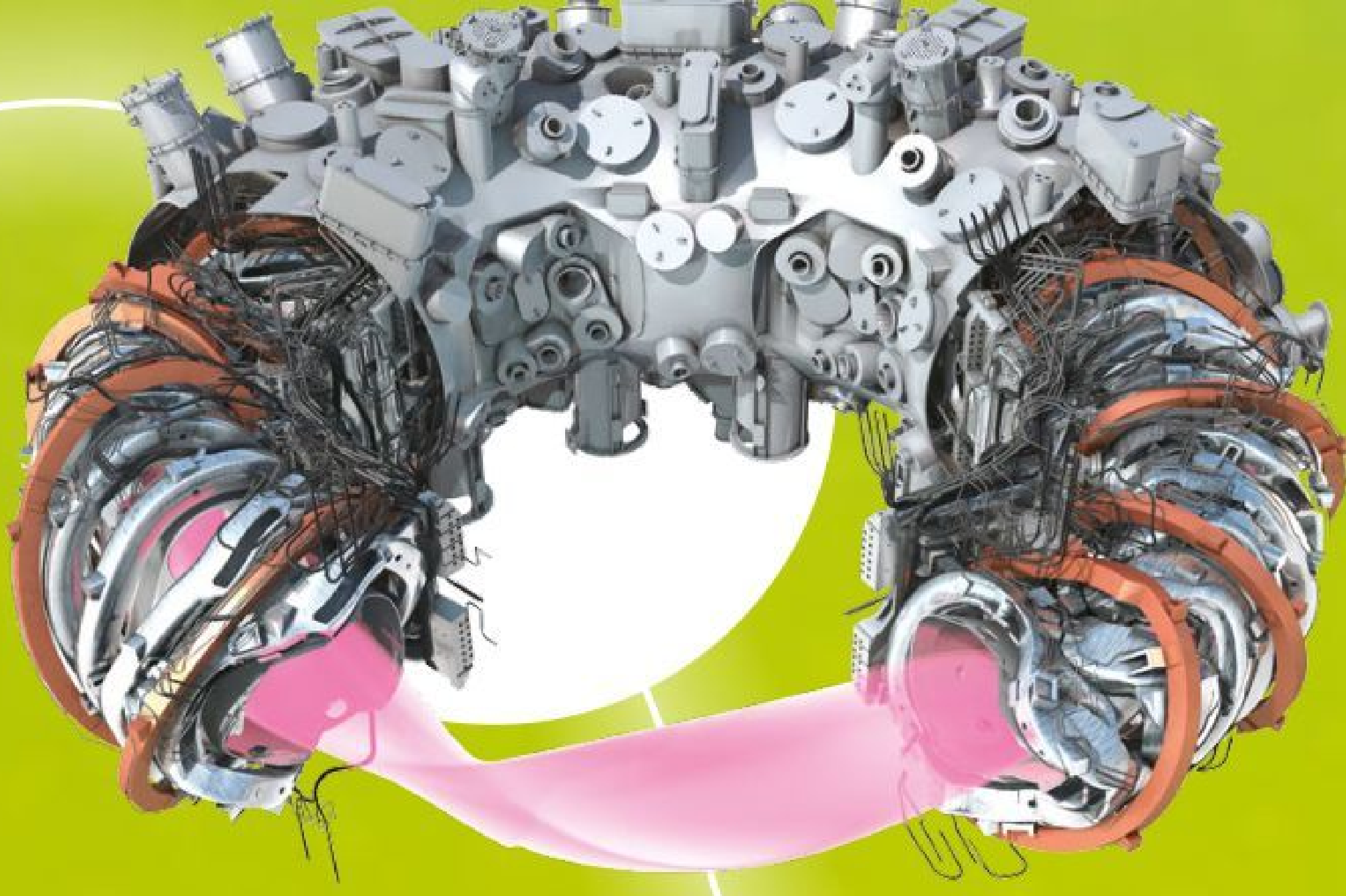
FUTURE OF SCIENCE



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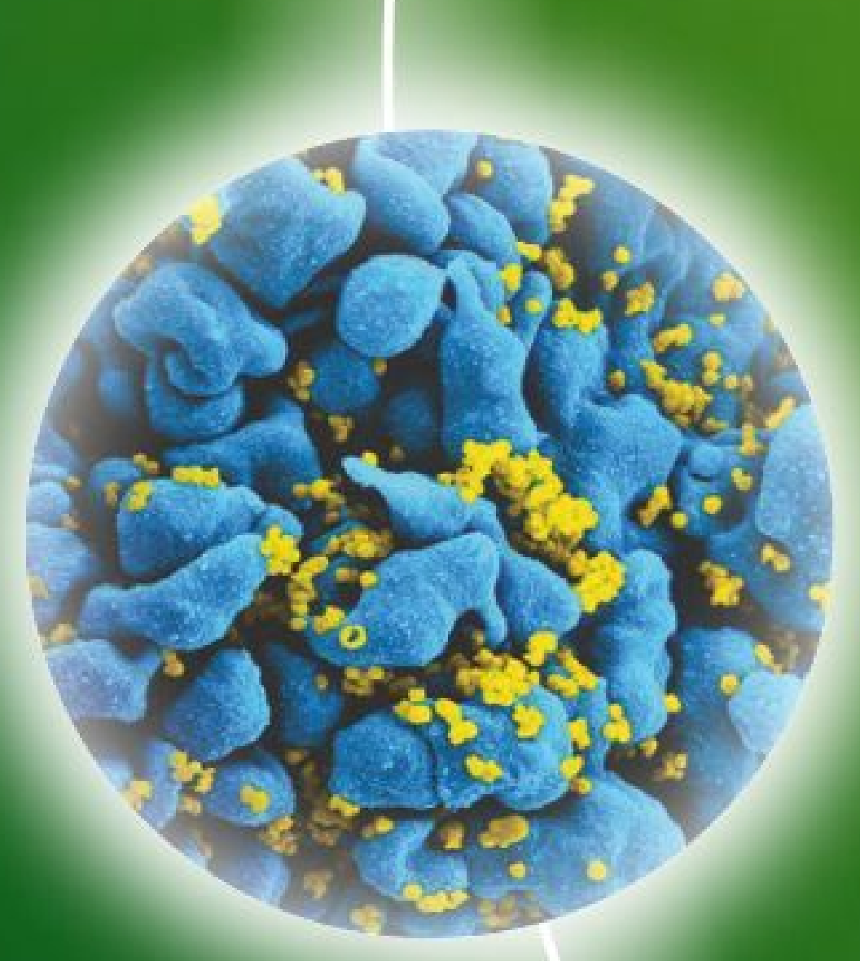

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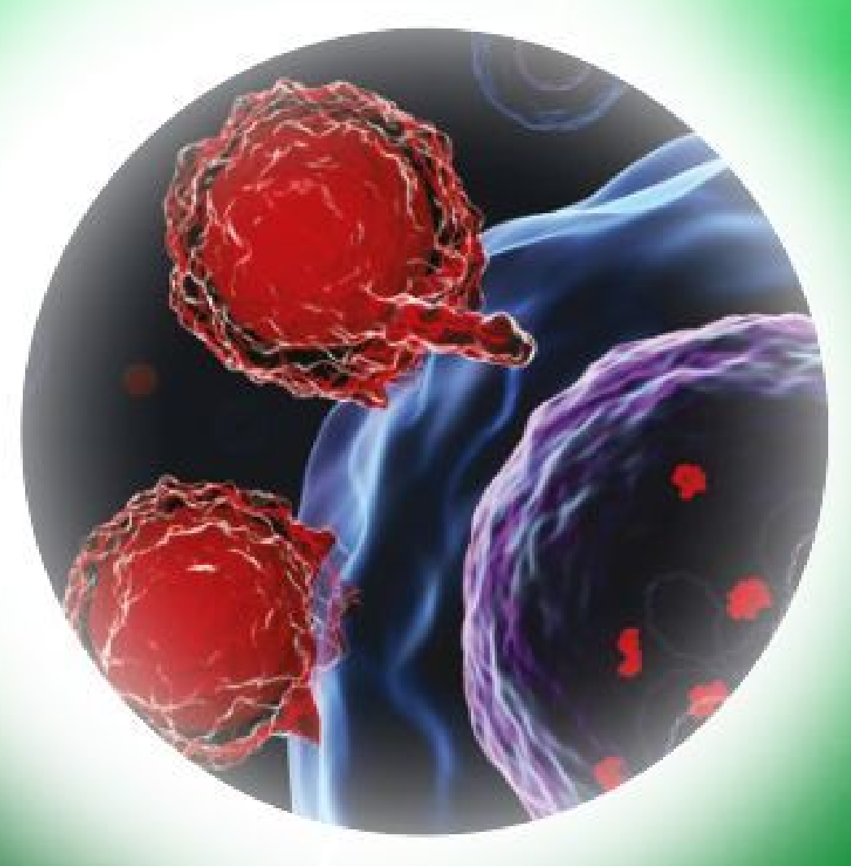

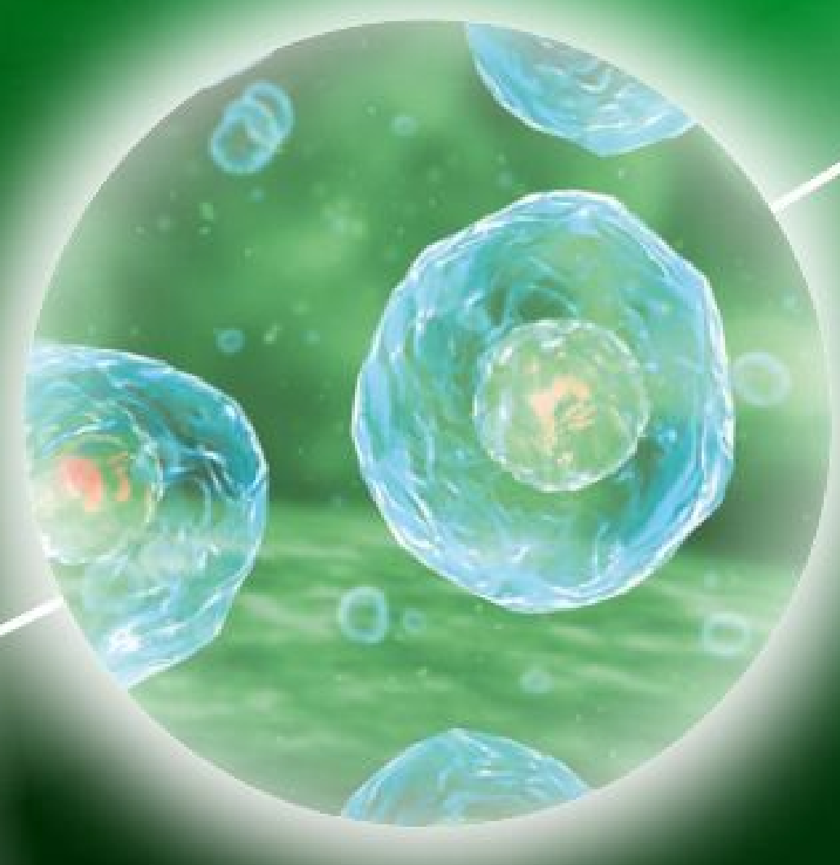

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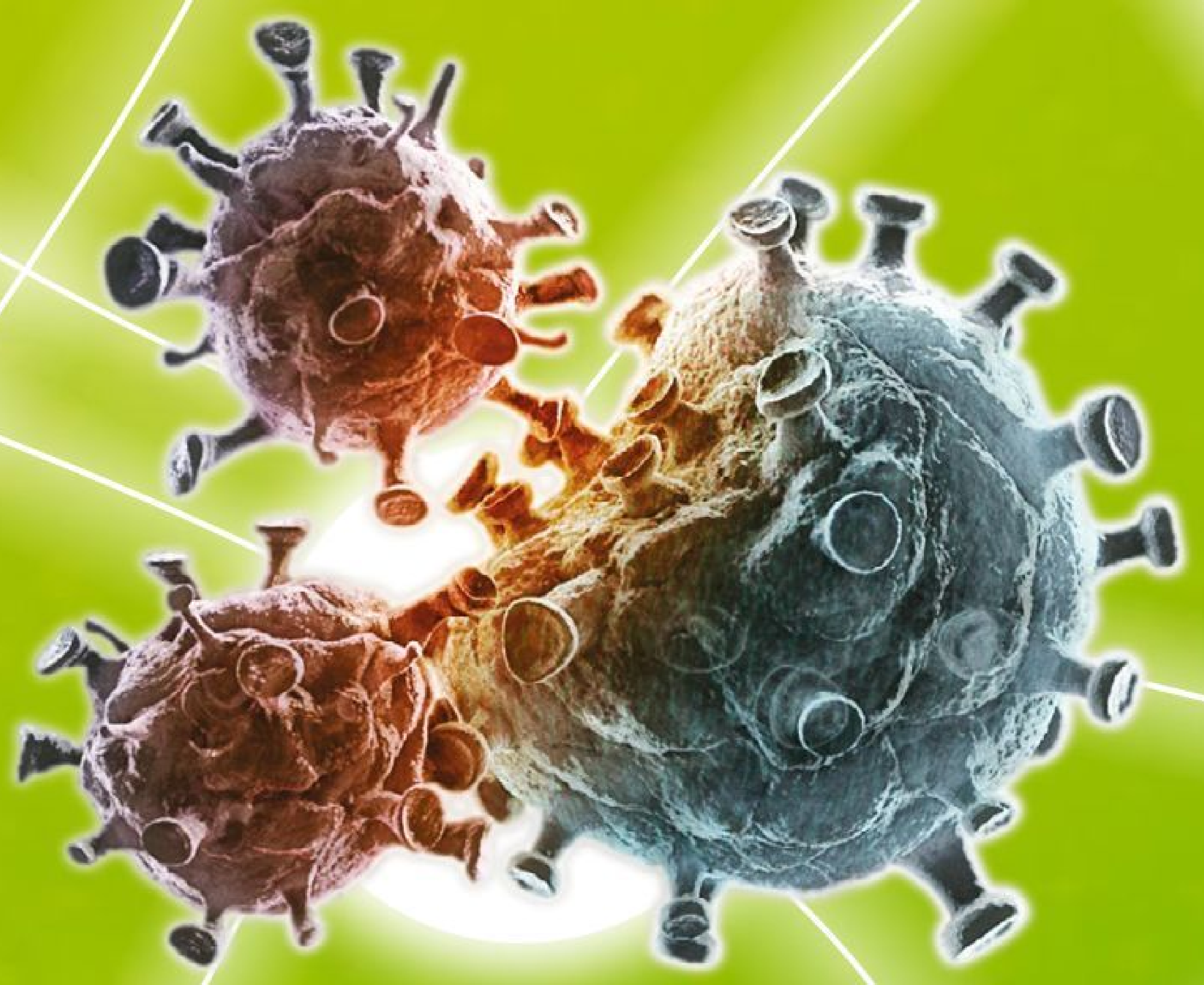

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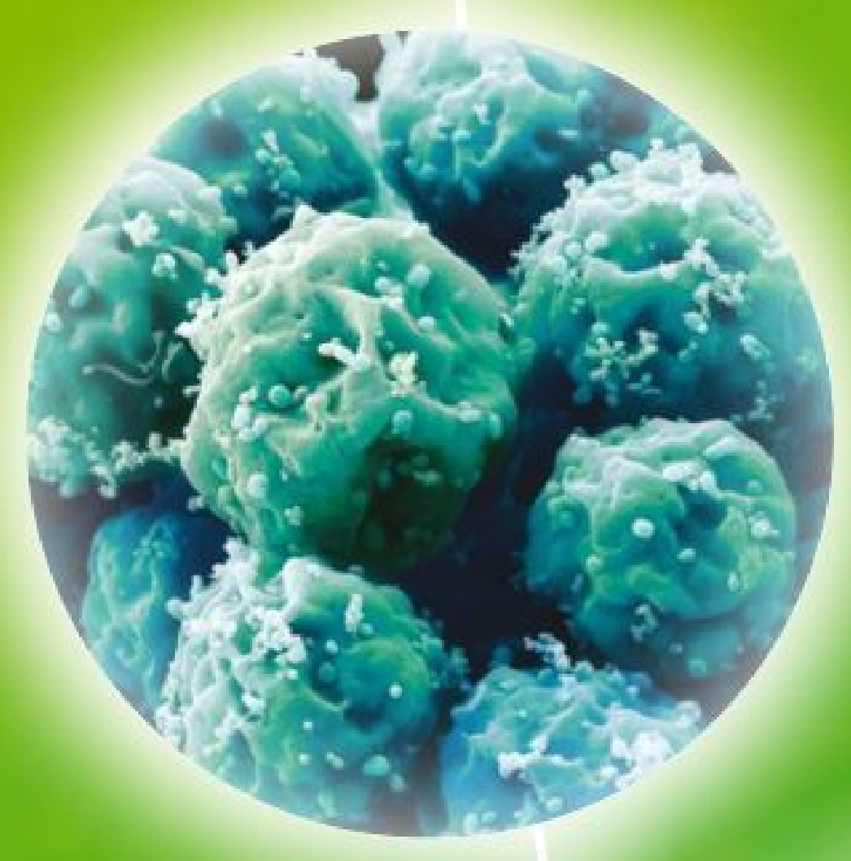

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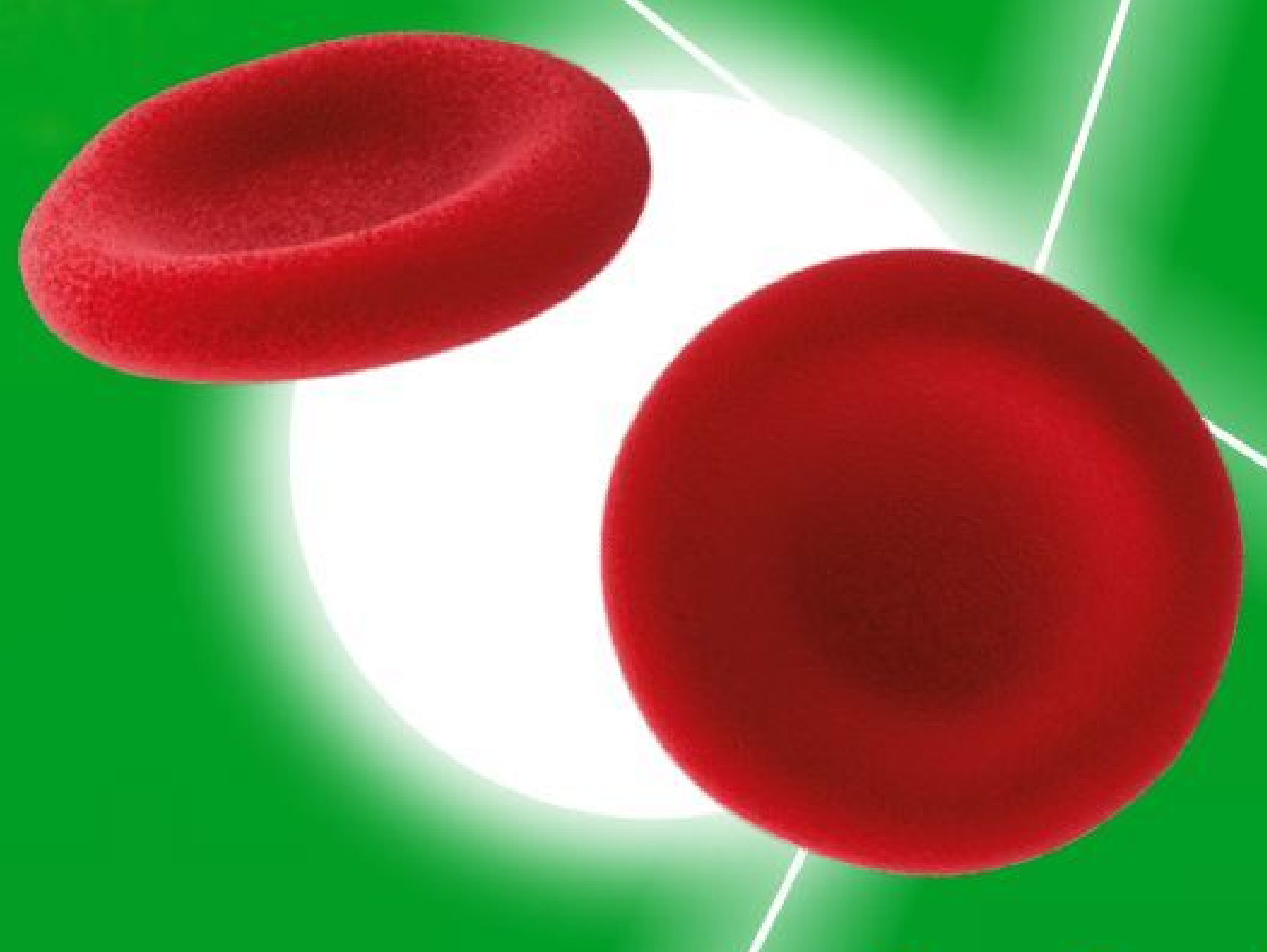

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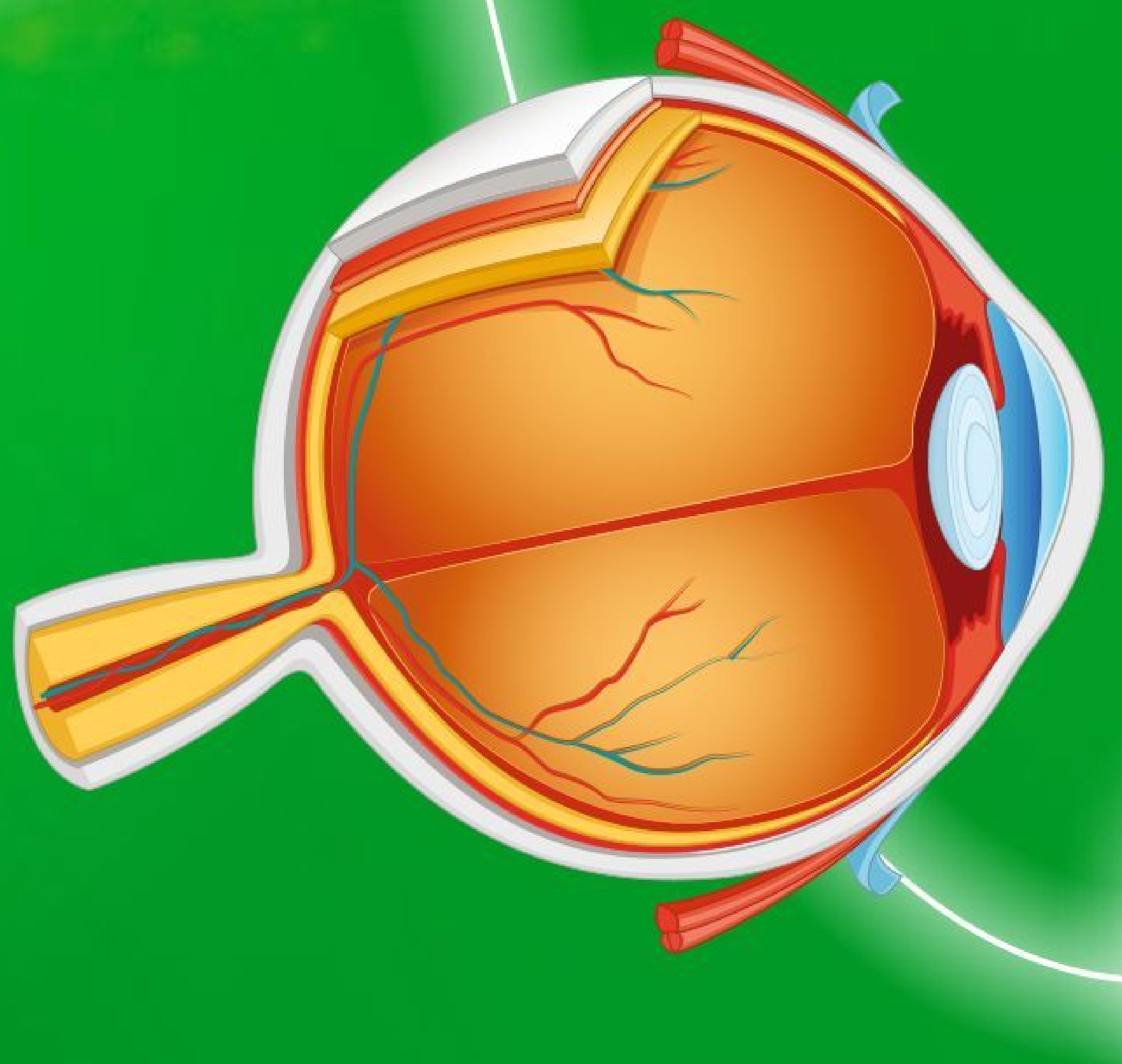

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NUCLEAR POWER

INVESTIGATE HOW TODAY'S NUCLEAR POWER STATIONS WORK AND DELVE INTO THE PROMISE OF NUCLEAR FUSION

The idea of harnessing energy from nuclear reactions to generate electricity is over 60 years old. Following a slow-down in the 1970s, nuclear power is now on the rise again, partially in response to concerns over the harmful effects of burning fossil fuels. Today's commercial nuclear reactors generate energy from the process of nuclear fission, and we'll investigate what that means, why it generates so much energy and how a nuclear power station works. However, while fission is a tried and proven technology, many scientists believe that the future is one of nuclear fusion. Over the next few pages, we'll take a look at that process to see how it differs from fission and how far we are from generating power from this potentially abundant energy source.

Chemical bonds contain a large amount of energy, which can be released by chemical reactions. Burning fossil fuels is a classic example, and the amount of energy that can be produced this way is evident if we think about how far a car can travel when a gallon of petrol is oxidised. But the amount of energy stored in chemical bonds is tiny compared to the amount of energy that is stored in the bonds between the protons and neutrons in the nucleus of an atom.

It is this energy that is released in the nuclear reactions that take place in nuclear power plants, and the benefit compared to burning fossil fuels is staggering. Weight for weight, fission of nuclear fuel can produce 2-3 million times more energy than burning coal or oil.

FISSION VS FUSION

Fission and fusion are opposite nuclear reactions, but both can generate energy

FISSION REACTION

Fission is brought about when a neutron collides with a high atomic weight nucleus such as uranium-235.

FISSION PRODUCTS

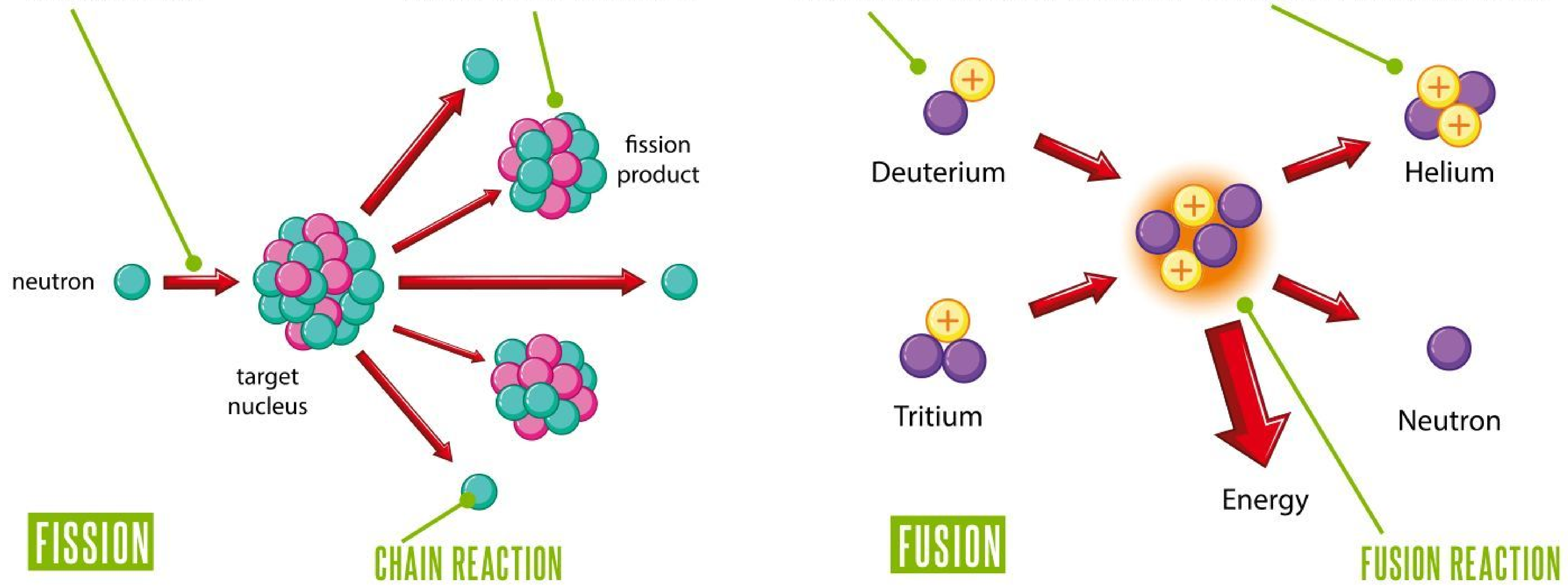
The result is two smaller nuclei – often barium and krypton in the case of uranium-235 fission – plus two or three neutrons.

DEUTERIUM AND TRITIUM

Deuterium nuclei contain one proton (yellow) and one neutron (purple). Tritium nuclei have an extra neutron.

FUSION PRODUCTS

Fusion generates a nucleus of a larger element (helium) and a neutron is emitted. Energy is released in the process.

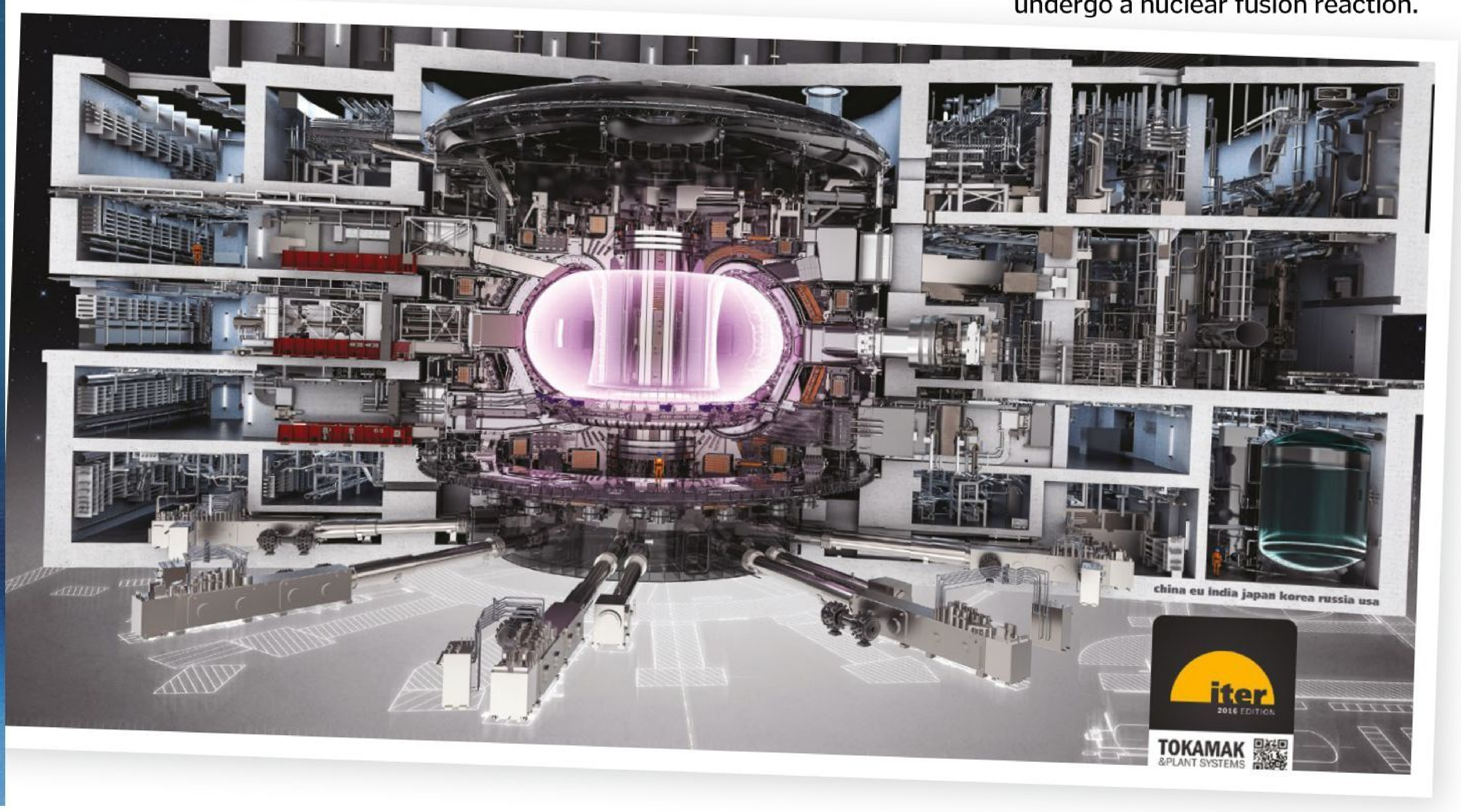


CHAIN REACTION

More neutrons are generated than the one taken to initiate the fission. These reach other uranium-235 nuclei, resulting in a chain reaction.

FUSION REACTION

When brought together at over 100 million degrees Celsius, the deuterium and tritium nuclei undergo a nuclear fusion reaction.



⬡ The ITER project aims to deliver the first large-scale fusion reactor by 2035

> *"Although the atom was once thought to be indivisible, nuclear fission involves splitting it"*

BINDING ENERGY

The binding energy is the energy required to separate a pair of nucleons (ie protons and neutrons). It varies with the number of nucleons in the nucleus (the atomic weight), rising to a maximum between about 50 and 70 nucleons. Because both the large fissile (capable of fission) nuclei and the small fusile (capable of fusion) nuclei have a smaller binding energy than that of the nuclei they become during fission or fusion, energy is released in the reaction.

The shape of the graph also explains why more energy is available from fusion than fission. Due to the particularly steep curve for small numbers of nucleons, there is a large difference between the binding energy of fusile nuclei (2H and 3H) and that of the result of the fusion (4He).

ENERGY RELEASE

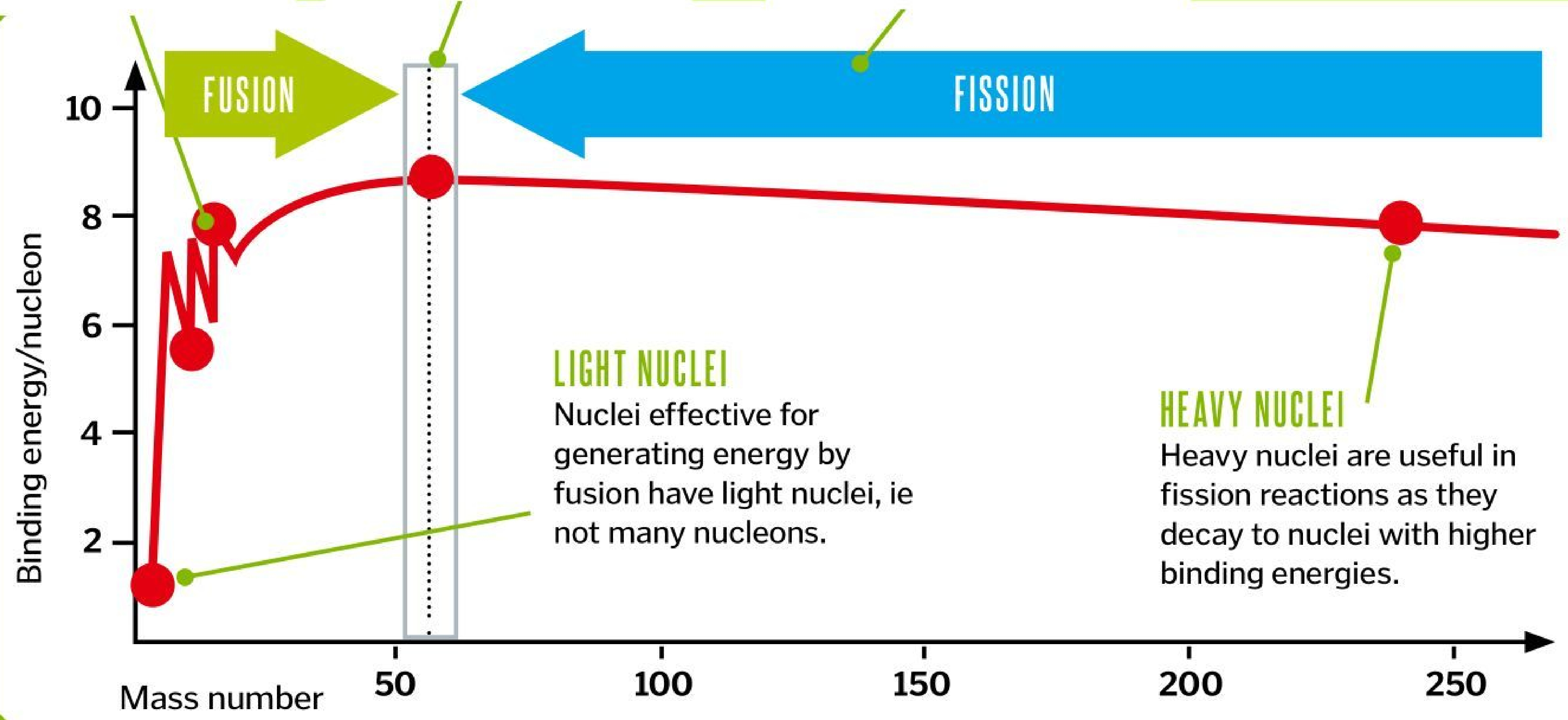
Fusion causes light nuclei to become nuclei with a higher binding energy, releasing energy.

STABLE REGION

Iron and the elements close to it in terms of atomic mass have tightly-bound nuclei.

FISSION OR FUSION?

Lighter elements release energy by fusion, while heavier elements release it by fission.



LIGHT NUCLEI

Nuclei effective for generating energy by fusion have light nuclei, ie not many nucleons.

HEAVY NUCLEI

Heavy nuclei are useful in fission reactions as they decay to nuclei with higher binding energies.

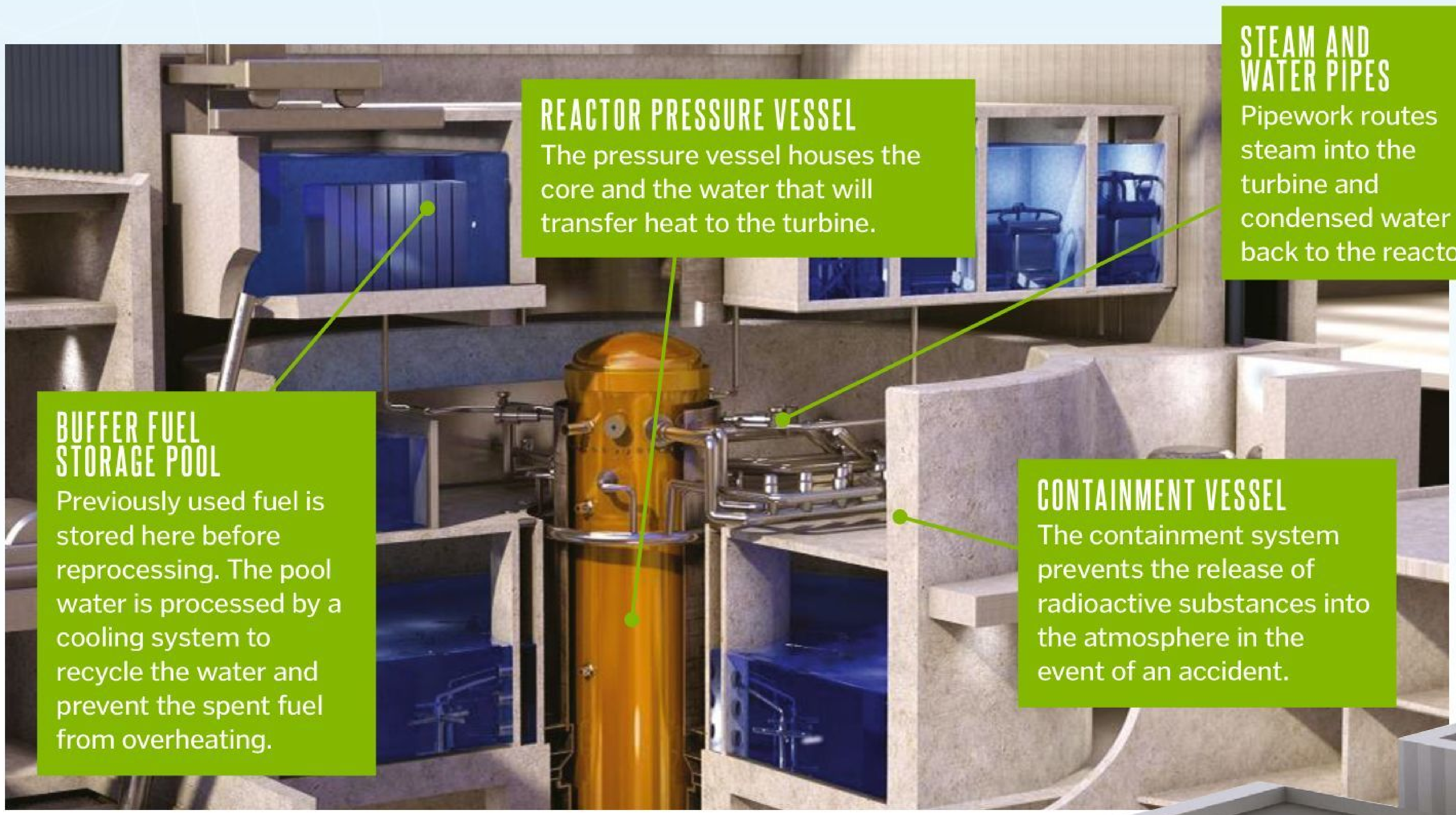
© Shutterstock; Nuclear Regulatory Commission; ITER Organization, http://www.iter.org

However, elements can exist in several forms, known as isotopes, which differ in the number of neutrons in their nucleus. Uranium isotopes include uranium-235 (otherwise denoted as 235U) and uranium-238 (238U), where the number is the atomic weight, which is the sum of the number of protons and neutrons. Naturally occurring uranium is about 99.27 per cent uranium-238 and only 0.7 per cent uranium-235 – not particularly useful for energy generation because uranium-235 is the isotope that can undergo fission (uranium-238 cannot sustain a fission chain reaction). To be useful as a fuel, therefore, the concentration of the fissile uranium-235 has to be increased in a process called enrichment. Because the chemical properties of the two main isotopes of uranium are very similar, enrichment is a lengthy process in which the concentration of uranium-235 is increased in steps. The enriched uranium used for power generation has about three to five per cent uranium-235.

Fission of uranium-235 occurs when neutrons are fired at it. The neutron is initially captured by the uranium-235, but this makes it highly unstable, causing it to split into two other elements, releasing energy in the process. Fission of uranium-235 can give rise to a whole range of by-products, although isotopes of barium and krypton are two of the most common. Most of these by-products are highly radioactive in themselves, so they, in turn, also decay. Crucially, though, the fission reaction also releases two or three neutrons, which are then free to collide with other uranium-235 atoms, and so cause them to undergo nuclear fission. This gives rise to a chain reaction, which means that the fusion reaction, once initiated, is self-sustaining. In fact, in a nuclear reactor, unless controlled, this process will result in the release of energy much too quickly, with disastrous consequences, as evidenced by the destruction of a reactor at the Chernobyl nuclear power station in Ukraine in 1986.

The solution is to use a material capable of neutron capture without itself undergoing fission, most commonly boron. These materials are fashioned into so-called control rods and housed in the reactor core. By raising and lowering the control rods, the neutron flux can be controlled to allow the fission reaction to take place while preventing a runaway situation, an eventuality called criticality. They also allow an emergency shut down of the reactor.

Discussion of nuclear power stations inevitably leads to talk of the various types of reactor, with names such as the pressurised water reactor, the boiling water reactor and the Magnox, or gas-cooled, reactor bandied around. At the highest level, though, all nuclear power



REACTOR PRESSURE VESSEL
The pressure vessel houses the core and the water that will transfer heat to the turbine.

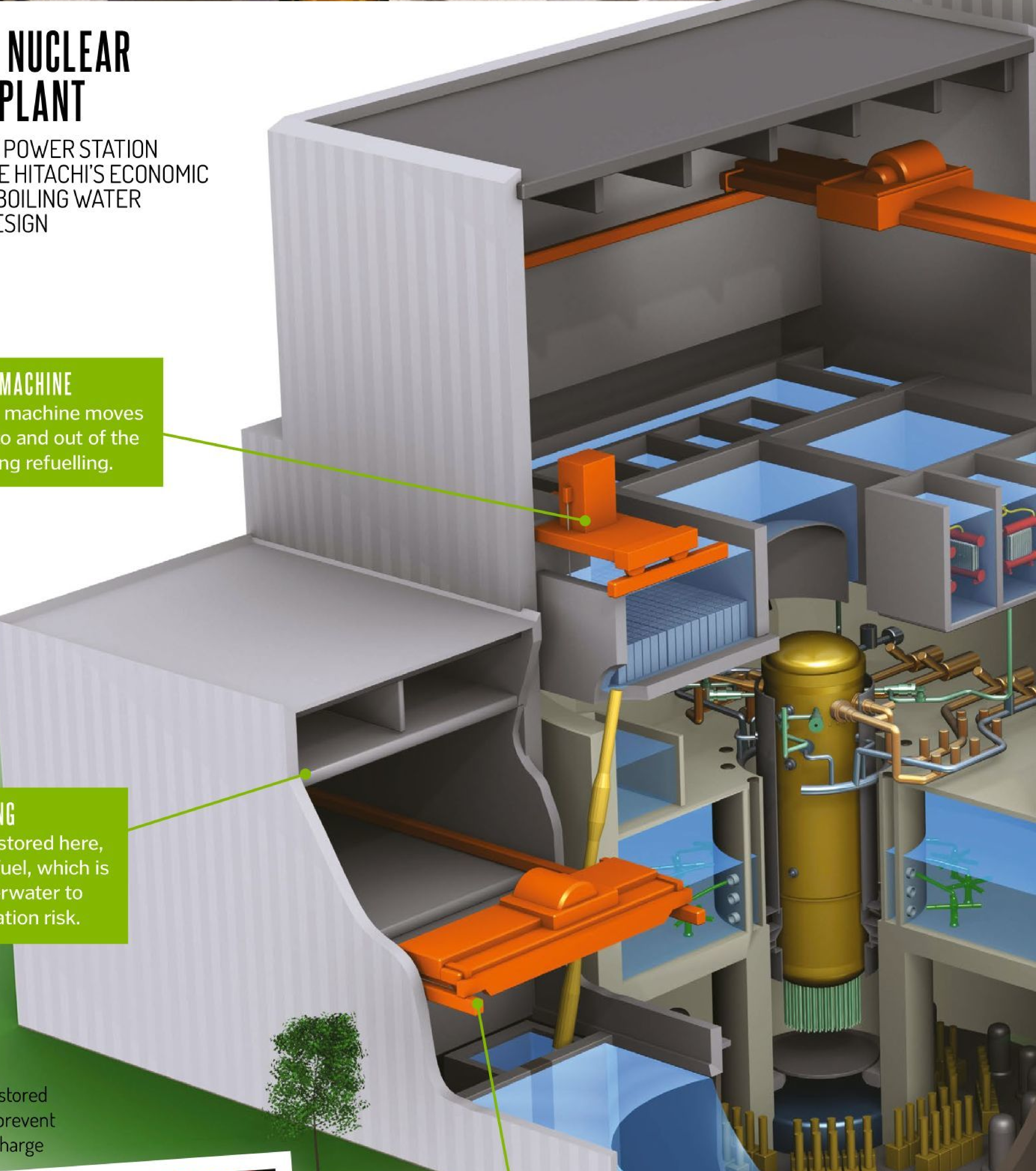
STEAM AND WATER PIPES
Pipework routes steam into the turbine and condensed water back to the reactor.

BUFFER FUEL STORAGE POOL
Previously used fuel is stored here before reprocessing. The pool water is processed by a cooling system to recycle the water and prevent the spent fuel from overheating.

CONTAINMENT VESSEL
The containment system prevents the release of radioactive substances into the atmosphere in the event of an accident.

INSIDE A NUCLEAR FISSION PLANT

A TOUR OF A POWER STATION BASED ON GE HITACHI'S ECONOMIC SIMPLIFIED BOILING WATER REACTOR DESIGN

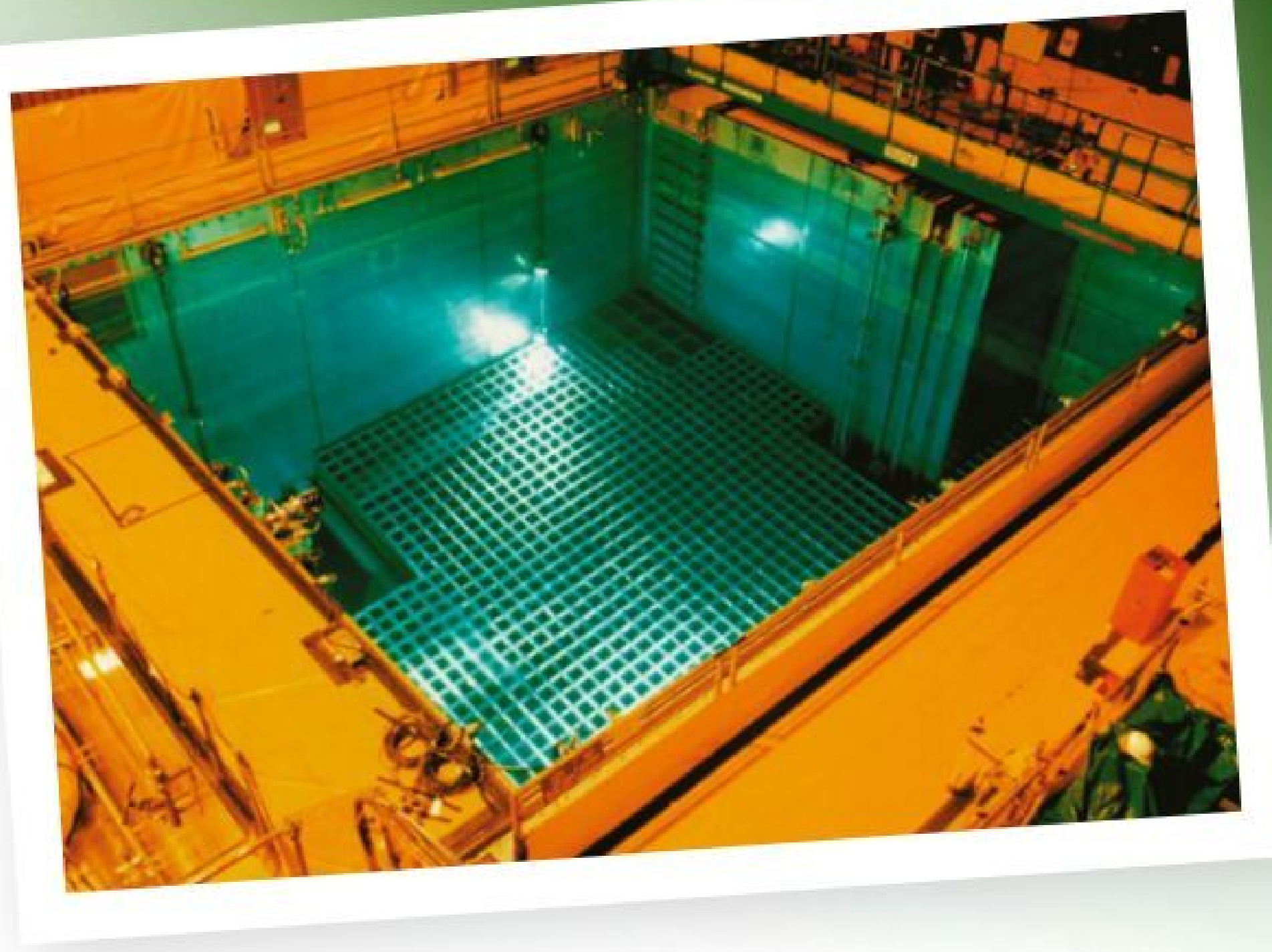


REFUELLING MACHINE
This robotic machine moves fuel rods into and out of the reactor during refuelling.

FUEL BUILDING
New fuel is stored here, as is spent fuel, which is stored underwater to reduce radiation risk.

INCLINED FUEL TRANSFER SYSTEM
The inclined fuel transfer system transfers new and used fuel between the fuel building and the containment vessel.

○ Spent fuel is stored underwater to prevent radioactive discharge

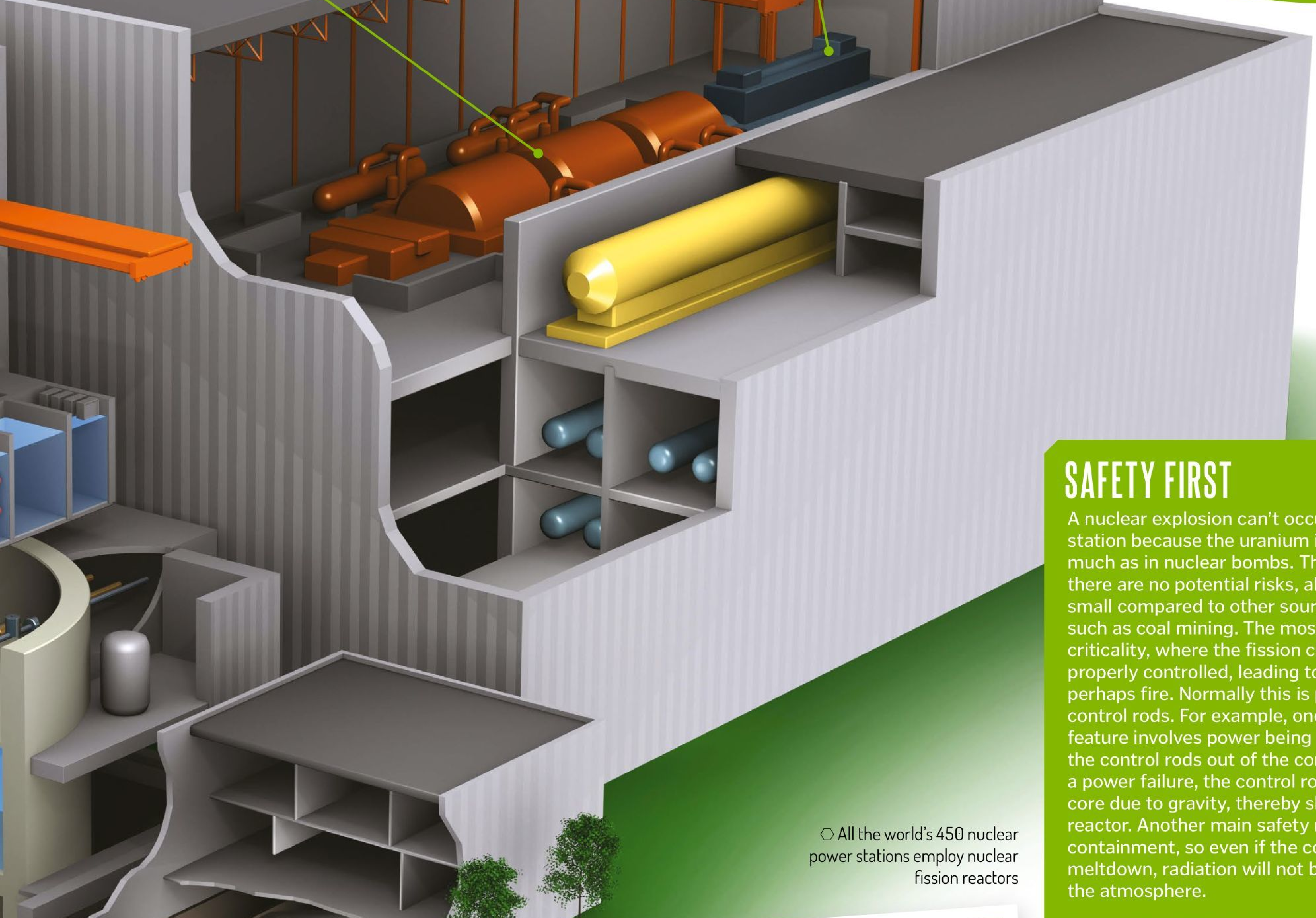


> “The difference between reactor types relates to the way the heat is extracted from the core”

Sandia Laboratory’s Z Machine is used for researching high temperatures and pressures as needed for nuclear fusion

GENERATOR
Sharing a drive shaft with the turbine, the generator converts the mechanical energy into electrical energy.

STEAM TURBINE
As in oil- or coal-fired power stations, the turbine converts the thermal energy in the steam into rotational mechanical energy.



CONTROL ROOM
Although automated systems play a role, operators in the control room can monitor and control power station operations.

All the world’s 450 nuclear power stations employ nuclear fission reactors

SAFETY FIRST

A nuclear explosion can’t occur in a power station because the uranium isn’t enriched as much as in nuclear bombs. This isn’t to say there are no potential risks, although they’re small compared to other sources of energy, such as coal mining. The most obvious risk is criticality, where the fission chain reaction isn’t properly controlled, leading to overheating and perhaps fire. Normally this is prevented using control rods. For example, one clever safety feature involves power being needed to hold the control rods out of the core. In the event of a power failure, the control rods fall into the core due to gravity, thereby shutting down the reactor. Another main safety measure is containment, so even if the core suffers a meltdown, radiation will not be released into the atmosphere.

Control rods are essential in preventing criticality from occurring in a nuclear reactor

© NRC; GE; Sandia Labs; Getty

stations work in much the same way. The nuclear fission reaction generates heat, the heat turns water into steam and, from here on, things are the same as in a coal- or oil-fired power station. The steam drives a turbine, which in turn drives a generator that produces electricity.

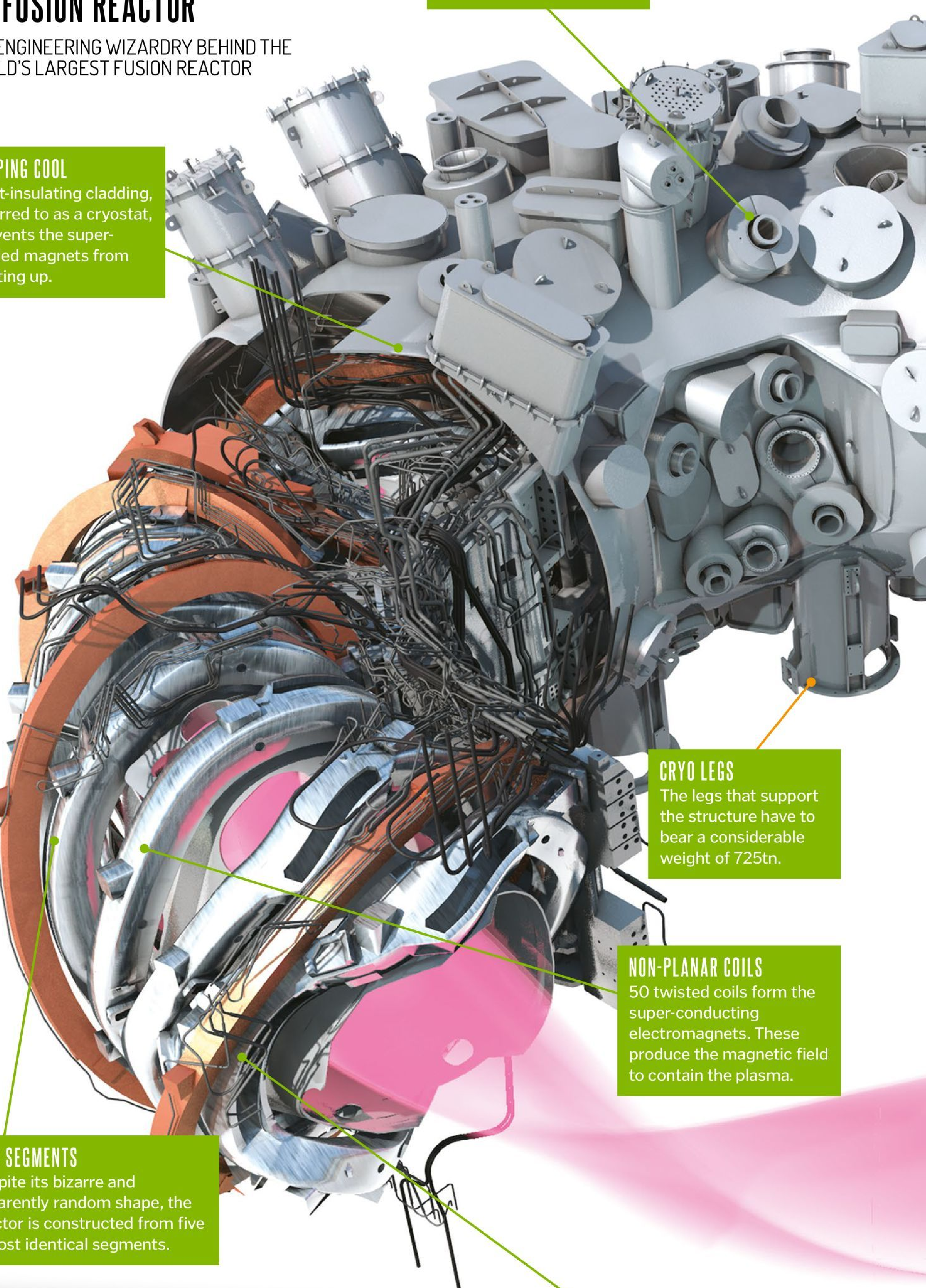
The difference between the various reactor types relates to the way the heat is extracted from the core. In the boiling water reactor, the water that is heated to produce the steam is pumped through the nuclear reactor. In the pressurised water reactor, on the other hand, to prevent contaminated steam entering the turbine, there are two water circuits. The primary water flows through the reactor, which gives up its heat to the secondary water in a heat exchanger, the secondary water turning to steam and driving the turbine. The advanced gas-cooled reactor, as favoured in the UK, is similar except that the primary circuit, which transfers heat from the reactor to the water in the secondary circuit, uses carbon dioxide instead.

So much for the current state of play, but the Holy Grail of nuclear power is fusion rather than fission. As the name suggests, nuclear fusion is the opposite of nuclear fission – two atomic nuclei merging to produce an element with a larger atomic mass. Again this generates energy; the plentiful energy that the Earth receives from the Sun is the result of a massive nuclear fusion reaction. One of the Sun's fusion reactions, and the one that has been the subject of most research, occurs between two isotopes of hydrogen, namely deuterium (hydrogen-2) and tritium (hydrogen-3) to produce helium. Fusion produces much more energy than fission and the by-products are not as radioactive, thereby reducing concerns over nuclear waste, plus the raw materials are potentially plentiful. Yet despite these benefits, there are some serious challenges to be met before fusion can form the basis for power generation. In particular, to initiate and maintain the reaction, temperatures of over 100 million degrees Celsius are needed, and to hold the deuterium and tritium atoms together a magnetic field thousands of times that of Earth's own is required.

Burning fossil fuels generates greenhouse gasses, but nuclear fission – while producing about 11 per cent of the world's electricity without producing carbon dioxide – has its critics. While renewables will undoubtedly play an important role in the future, the potential benefits of fusion, should it ever come to fruition, can't be ignored. Currently, a project involving China, the European Union, India, Japan, South Korea, Russia and the United States is causing considerable interest. Called ITER, the aim is to produce the first operating large-scale fusion reactor by 2035, so watch this space.

THE WENDELSTEIN 7-X FUSION REACTOR

THE ENGINEERING WIZARDRY BEHIND THE WORLD'S LARGEST FUSION REACTOR



PORTS
No fewer than 253 ports provide access to the centre of the reactor for monitoring and regulating the reaction process.

KEEPING COOL
Heat-insulating cladding, referred to as a cryostat, prevents the super-cooled magnets from heating up.

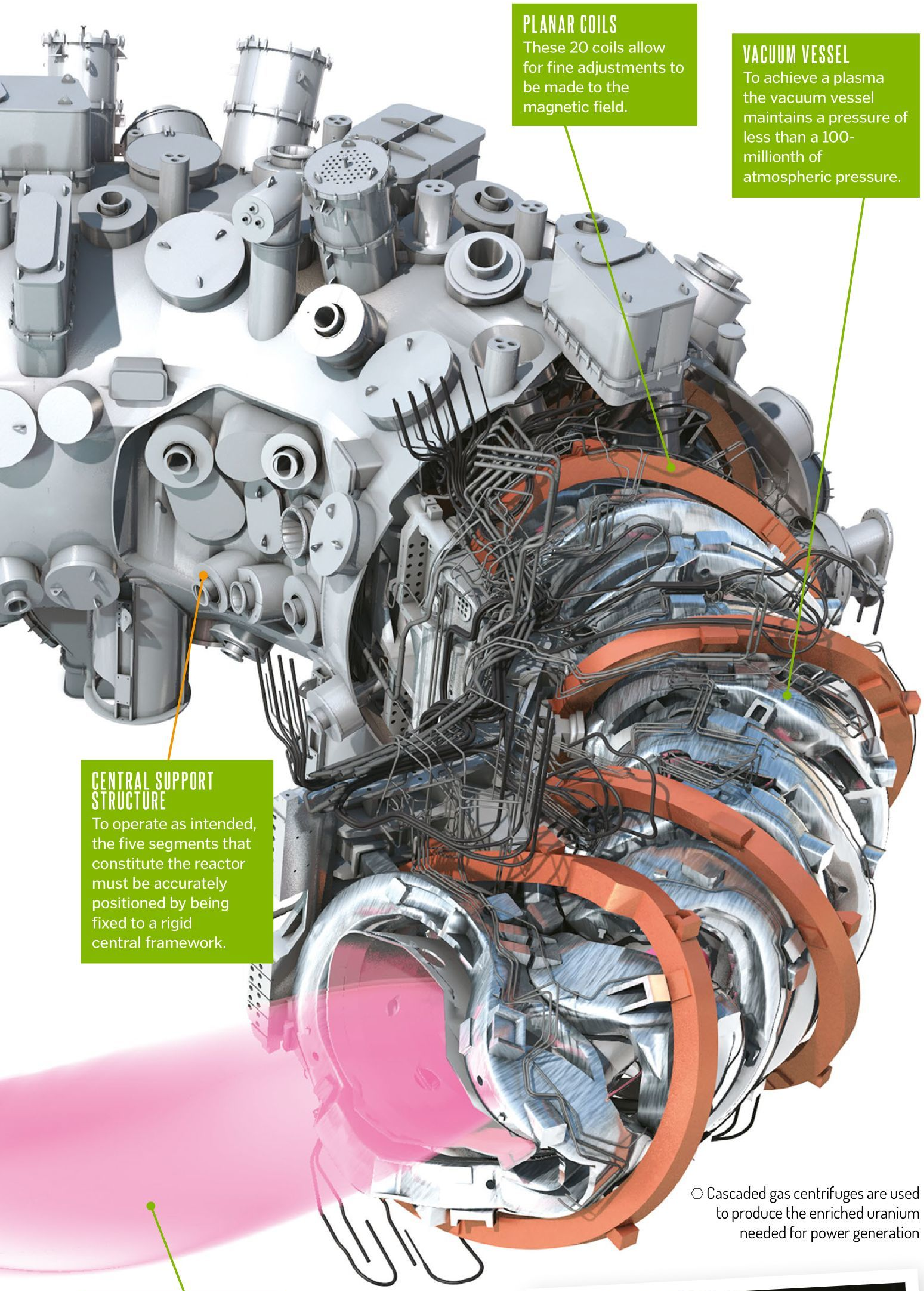
CRYO LEGS
The legs that support the structure have to bear a considerable weight of 725tn.

NON-PLANAR COILS
50 twisted coils form the super-conducting electromagnets. These produce the magnetic field to contain the plasma.

FIVE SEGMENTS
Despite its bizarre and apparently random shape, the reactor is constructed from five almost identical segments.

LIQUID HELIUM
Liquid helium at -270°C allows the loops that form the magnets to be superconductive.

○ The Rossing Mine in Namibia is one of the world's largest producers of uranium



PLANAR COILS
These 20 coils allow for fine adjustments to be made to the magnetic field.

VACUUM VESSEL
To achieve a plasma the vacuum vessel maintains a pressure of less than a 100-millionth of atmospheric pressure.

CENTRAL SUPPORT STRUCTURE
To operate as intended, the five segments that constitute the reactor must be accurately positioned by being fixed to a rigid central framework.

PLASMA
The isotopes for fusion are heated to 100 million degrees Celsius, at which temperature they form a plasma.

○ Cascaded gas centrifuges are used to produce the enriched uranium needed for power generation

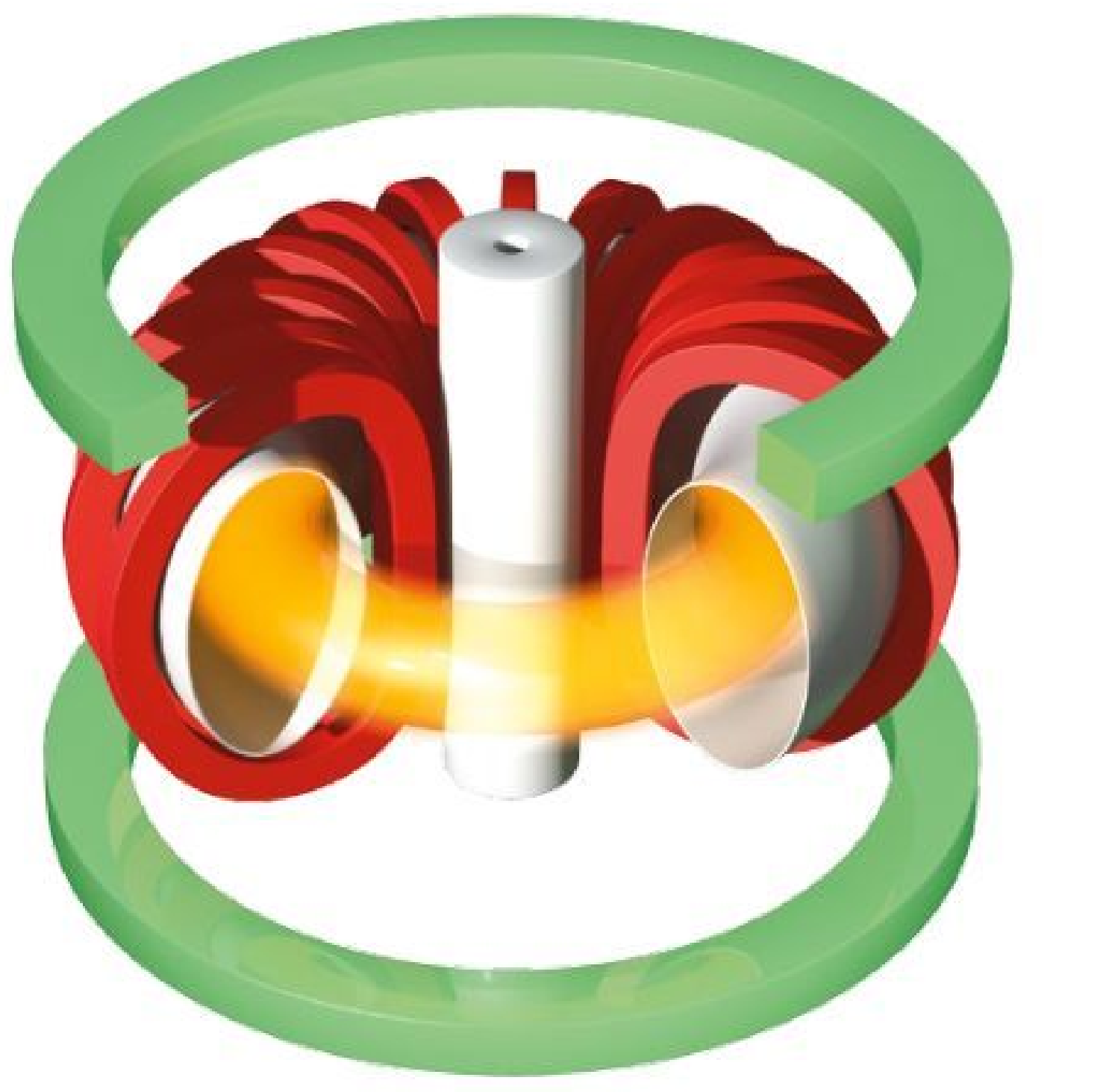
> *"The Holy Grail of nuclear power is fusion rather than fission"*

COMPARING ALTERNATIVE FUSION REACTORS

MOST FUSION REACTOR DESIGNS ARE TOROIDS WITH EXTERNAL COILS THAT GENERATE A MAGNETIC FIELD NEEDED TO PREVENT THE HIGH TEMPERATURE PLASMA FROM TOUCHING THE REACTOR WALLS. BUT THE MAGNETIC FIELD MUST HAVE A TWIST.

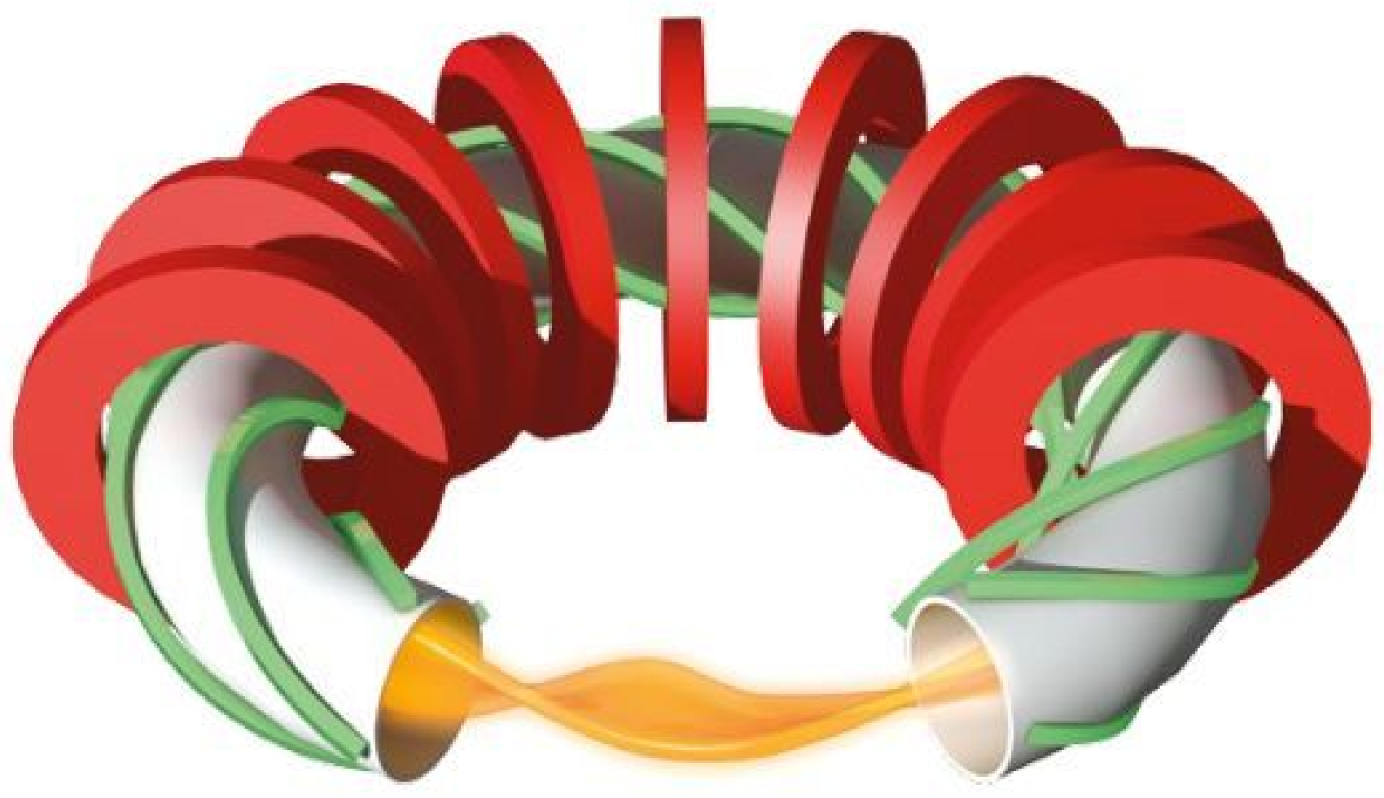
TOKAMAKS

In tokamak reactors, a current flows through the plasma to create the twist.



STELLARATORS

In stellarator reactors, the whole machine is twisted to achieve a twist in the field.



THE CHALLENGE OF FUSION

Research into nuclear fusion started decades ago and, for most of that time, commercial applications were thought to be 30 or 40 years away. So why are we getting no closer to a nuclear fusion power station? What's the challenge that's holding it at bay?

Unfortunately, there's no one single challenge but many. One of the most significant is that the necessary temperature is so high that large amounts of energy are needed. For many years experimental fusion reactors used more energy than they generated. A breakthrough came in 2014 at the Lawrence Livermore National Laboratory in the US, when a reactor generated 1.7 times more energy than it consumed. But the reactor was a small-scale device and the challenges are compounded as the technology is scaled up.

It's interesting to note that an aim of the ITER fusion reactor, scheduled for 2035, is to generate 500 megawatts but only use 50.

○ Lawrence Livermore's National Ignition Facility conducts fusion experiments using ultra-powerful lasers to heat and compress hydrogen fuel

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100 MILLION TIMES MORE POWERFUL THAN A LAPTOP

QUANTUM POWER

THE FUTURE OF COMPUTING AND HOW IT WILL CHANGE YOUR WORLD

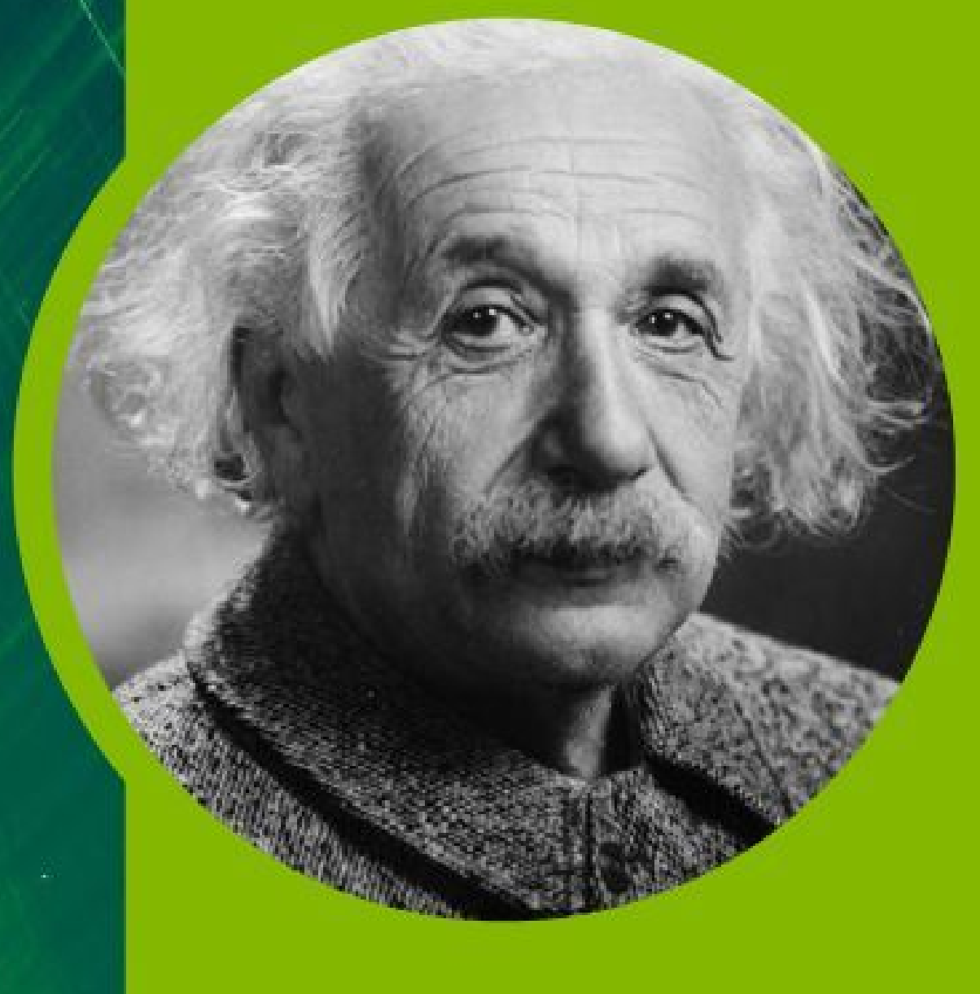
MEDICAL RESEARCH

QUANTUM TELEPORTATION

ADVANCED ENCRYPTION

THE PIONEERS OF QUANTUM MECHANICS

INTRODUCING THE PEOPLE WHO DARED TO THINK THE UNTHINKABLE, LAYING THE FOUNDATIONS OF QUANTUM TECHNOLOGY



ALBERT EINSTEIN
1905
Einstein explained the photoelectric effect by suggesting that light took the form of discrete bundles called photons. This seemed at odds with light's wave nature.

LOUIS DE BROGLIE
1923
French physicist Louis de Broglie expanded on previous discoveries by proposing that all tiny particles can behave as waves, and vice versa.

ERWIN SCHRÖDINGER
1926
Austrian physicist Erwin Schrödinger's paper describing the motion of an electron as a wave function was a defining moment in quantum mechanics.

WERNER HEISENBERG
1925-1927
Alongside Niels Bohr, Werner Heisenberg suggested that subatomic particles only adopt a particular state when observed.

ALEXANDER HOLEVO
1973
A Russian mathematician, Holevo was one of the researchers to lay the theoretical foundations of quantum mechanics.

It might be a term that trips off the tongue, and it may suggest a field of study dominated by the scientific elite, but quantum mechanics – or quantum physics if you prefer – is largely a mystery to the layperson. Surprisingly, therefore, it couldn't be much simpler to sum it up, even though understanding it is considerably more difficult.

Quantum mechanics is concerned with the behaviour of atoms, photons and the various subatomic particles, and it contrasts with classical physics, which describes the behaviour of everyday objects that are large enough to see.

The difference between classical physics and quantum mechanics is absolutely staggering. The objects that we see in the world around us behave in a way that seems intuitive, but once we start to consider very small objects, intuition and common sense have to be abandoned.

Instead, when we consider them individually, atoms, electrons and photons behave in a way that most people would be inclined to describe as impossible. That perception of impossibility isn't a naive view either. Even the eminent Nobel Prize-winning physicist Niels Bohr is on record as saying, "If anybody says he can think about quantum theory without getting giddy, it merely shows that he hasn't understood the first thing about it."

We'll look at some of these concepts in more detail in the boxout below, but, having made such an astonishing claim, it's surely only appropriate to provide a couple of examples of apparently impossible quantum behaviour.

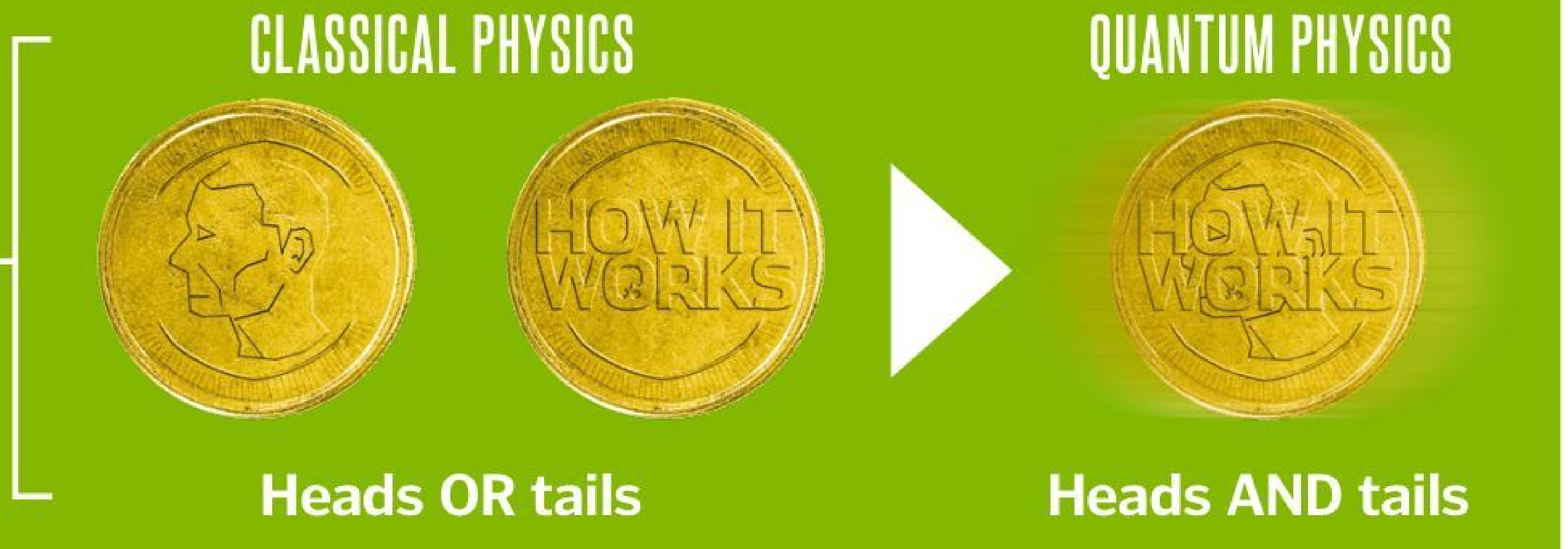
Perhaps one of the most bizarre things that can happen in the subatomic realm is that objects such as electrons or photons can be in two places at the same time or in two different

> *"The difference between classical physics and quantum mechanics is absolutely staggering"*

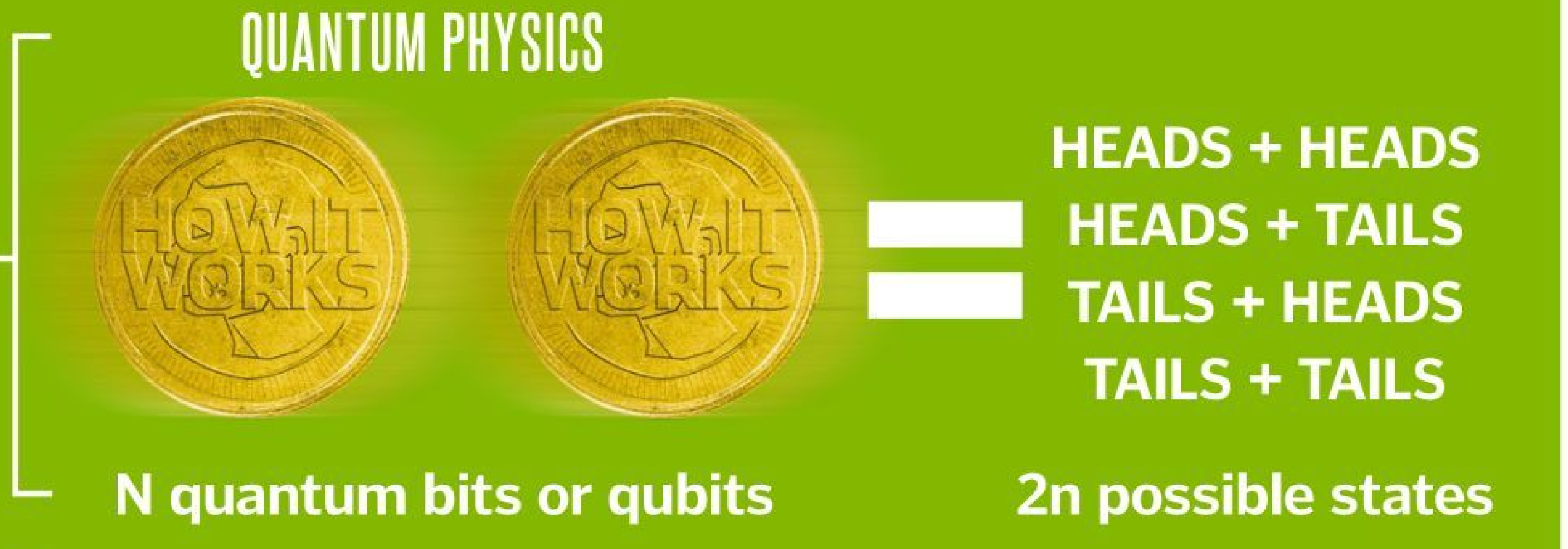
QUANTUM CONCEPTS

EXAMINING THE BIZARRE QUANTUM EFFECTS THAT UNDERPIN QUANTUM TECHNOLOGY

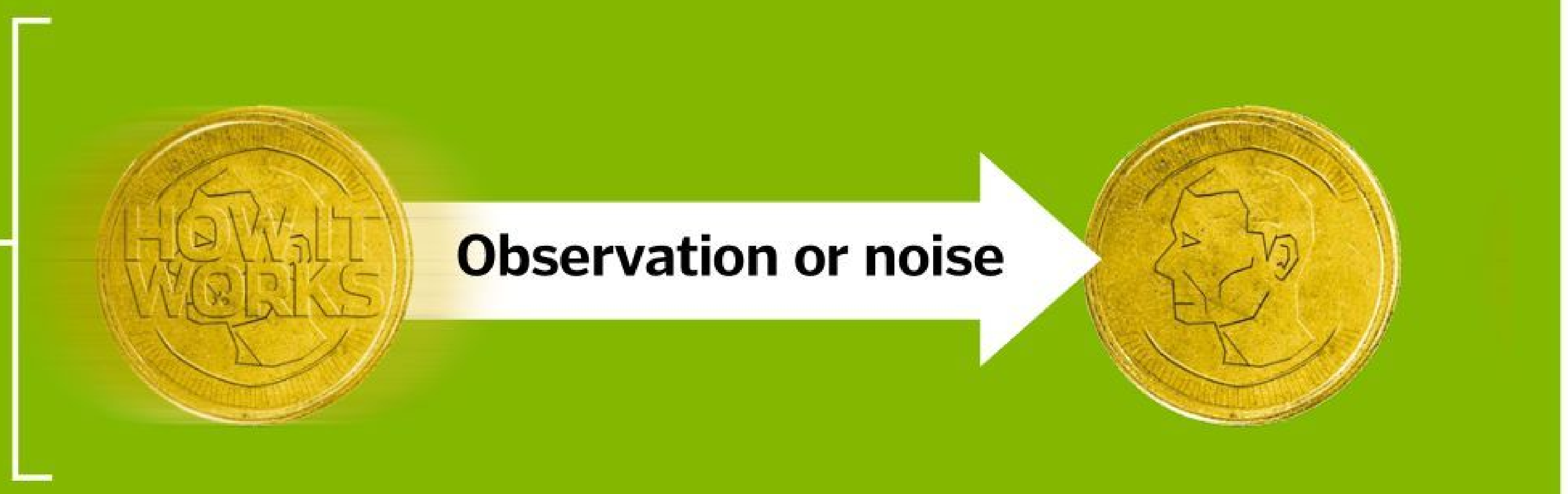
SUPERPOSITION
A particle in superposition is in two states at once, so it could represent both a binary 0 and 1. Think of a coin: if it's spinning you can see heads and tails simultaneously.



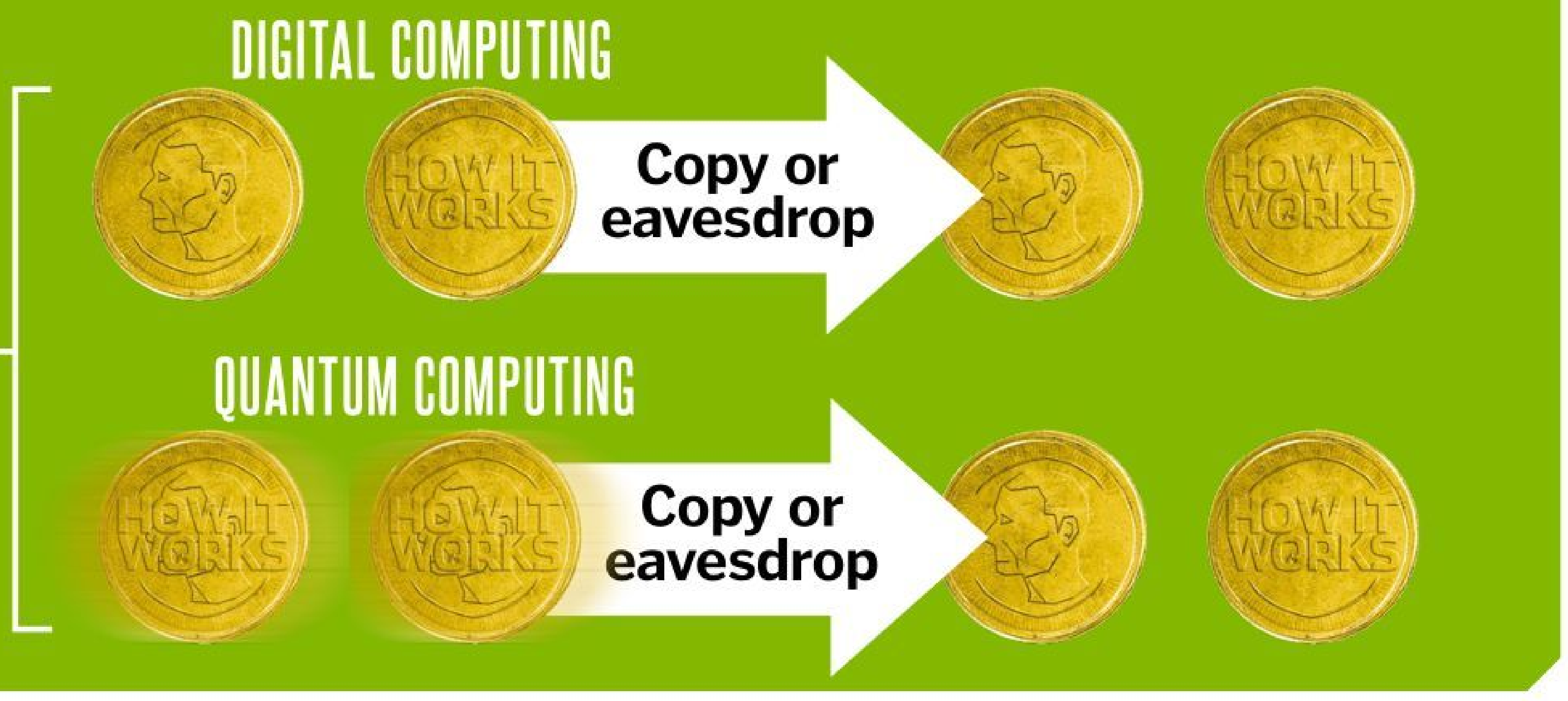
ENTANGLEMENT
Two entangled particles are strangely linked, so the fate of one affects the other. If you observe one particle this will cause its superposition to be lost, and the same will happen to its entangled twin.



OBSERVATION
Observing a particle in superposition causes it to adopt a single state. Any interaction with the environment does the same. The more entangled the particles, the harder it is to maintain superposition.



NO CLONING
Making a copy of a particle in superposition also causes the superposition to be lost. This makes designing a quantum computer tricky, but, in quantum communications, it alerts the sender to the presence of an eavesdropper.



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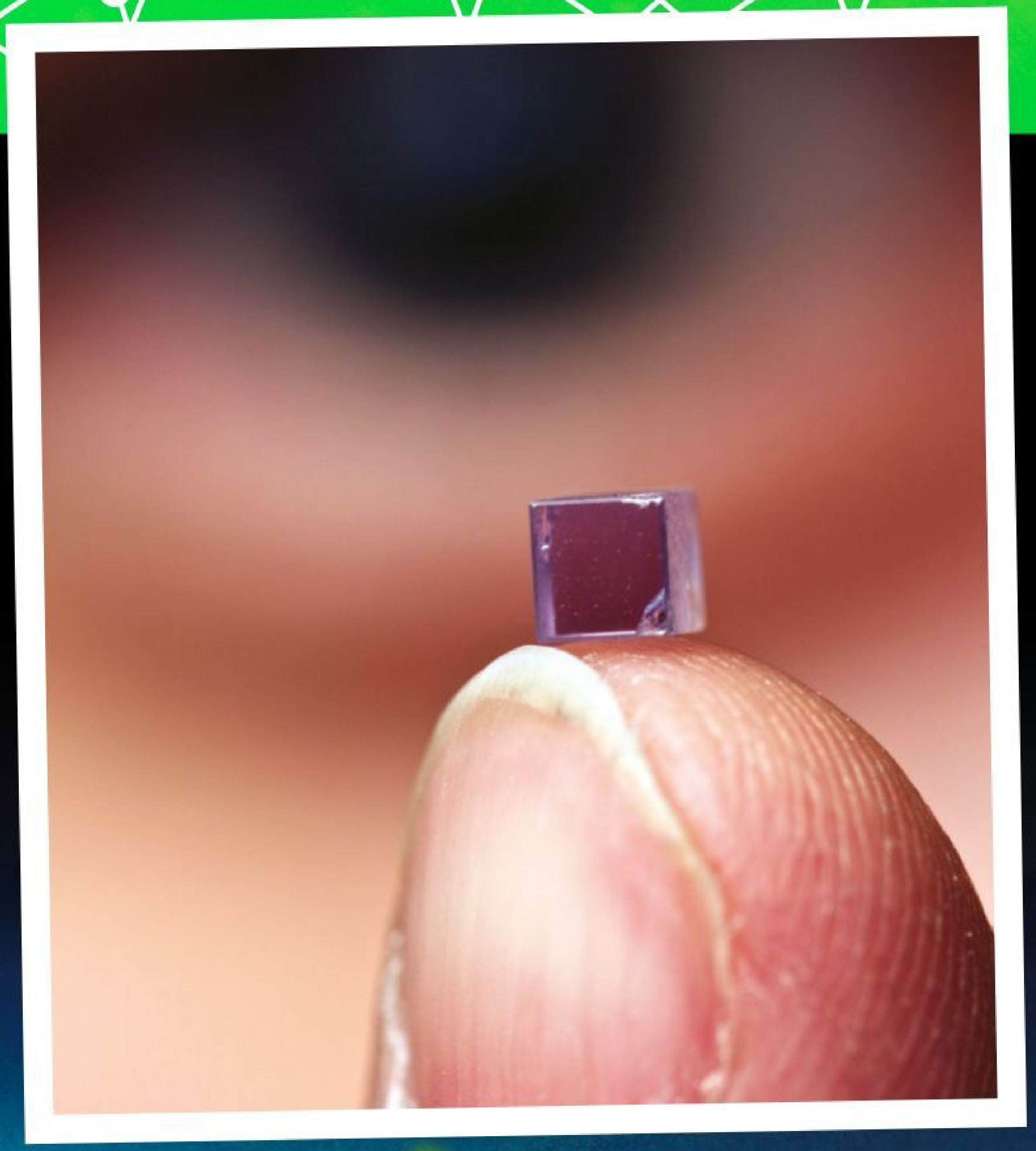
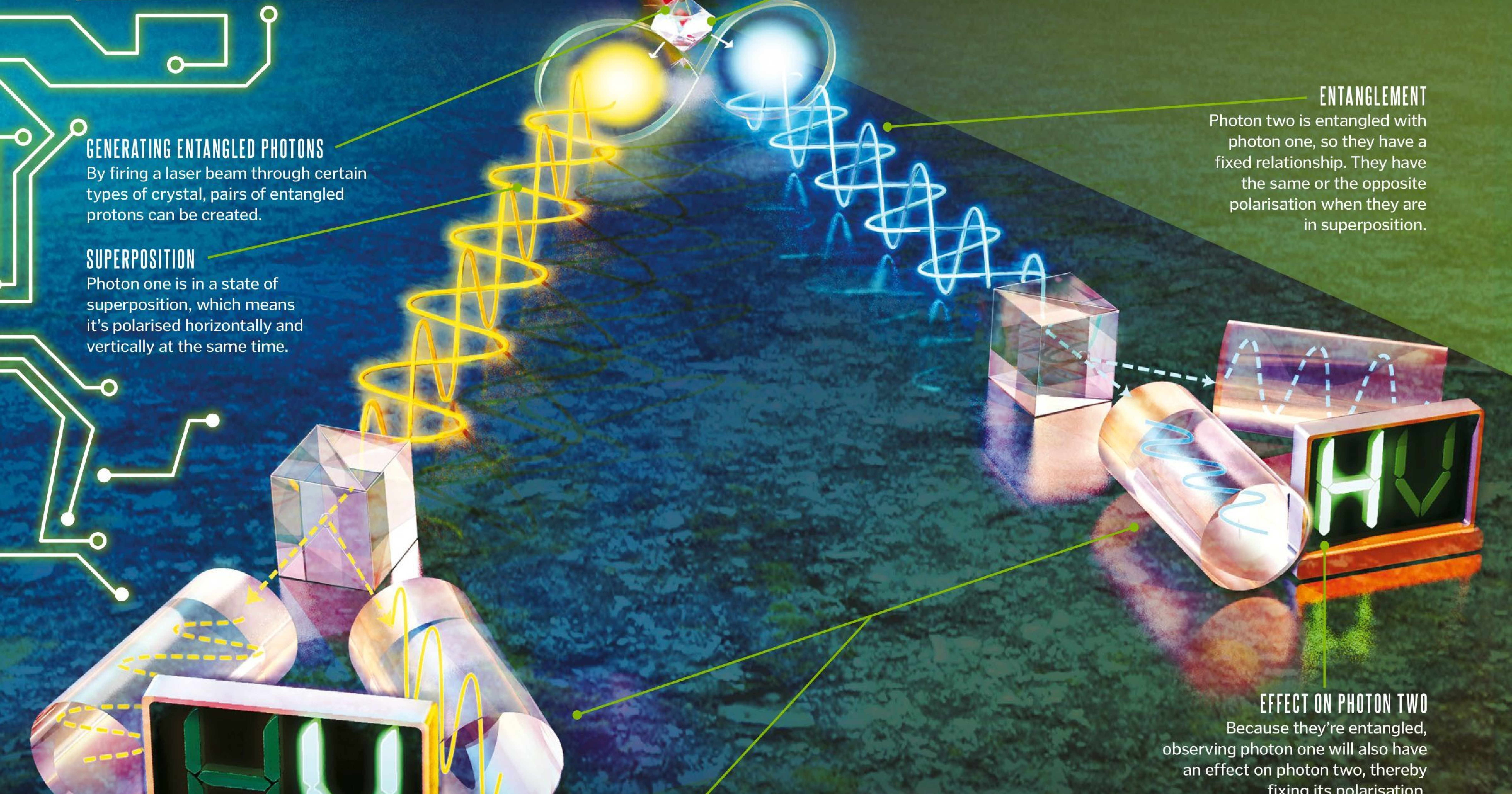
UNDERSTANDING QUANTUM ENTANGLEMENT

EXPERIMENTS HAVE CONFIRMED A QUANTUM EFFECT THAT EINSTEIN CALLED "SPOOKY"



○ Crystals doped with the rare element neodymium could potentially store quantum memories



SPLITTING THE BEAM

In this experiment a beam-splitter is used so that the two photons are dispatched to different destinations.

GENERATING ENTANGLED PHOTONS

By firing a laser beam through certain types of crystal, pairs of entangled protons can be created.

ENTANGLEMENT

Photon two is entangled with photon one, so they have a fixed relationship. They have the same or the opposite polarisation when they are in superposition.

SUPERPOSITION

Photon one is in a state of superposition, which means it's polarised horizontally and vertically at the same time.

EFFECT ON PHOTON TWO

Because they're entangled, observing photon one will also have an effect on photon two, thereby fixing its polarisation.

ACTION AT A DISTANCE

Observing one photon affects its entangled twin instantaneously, no matter how far apart the two photons are.

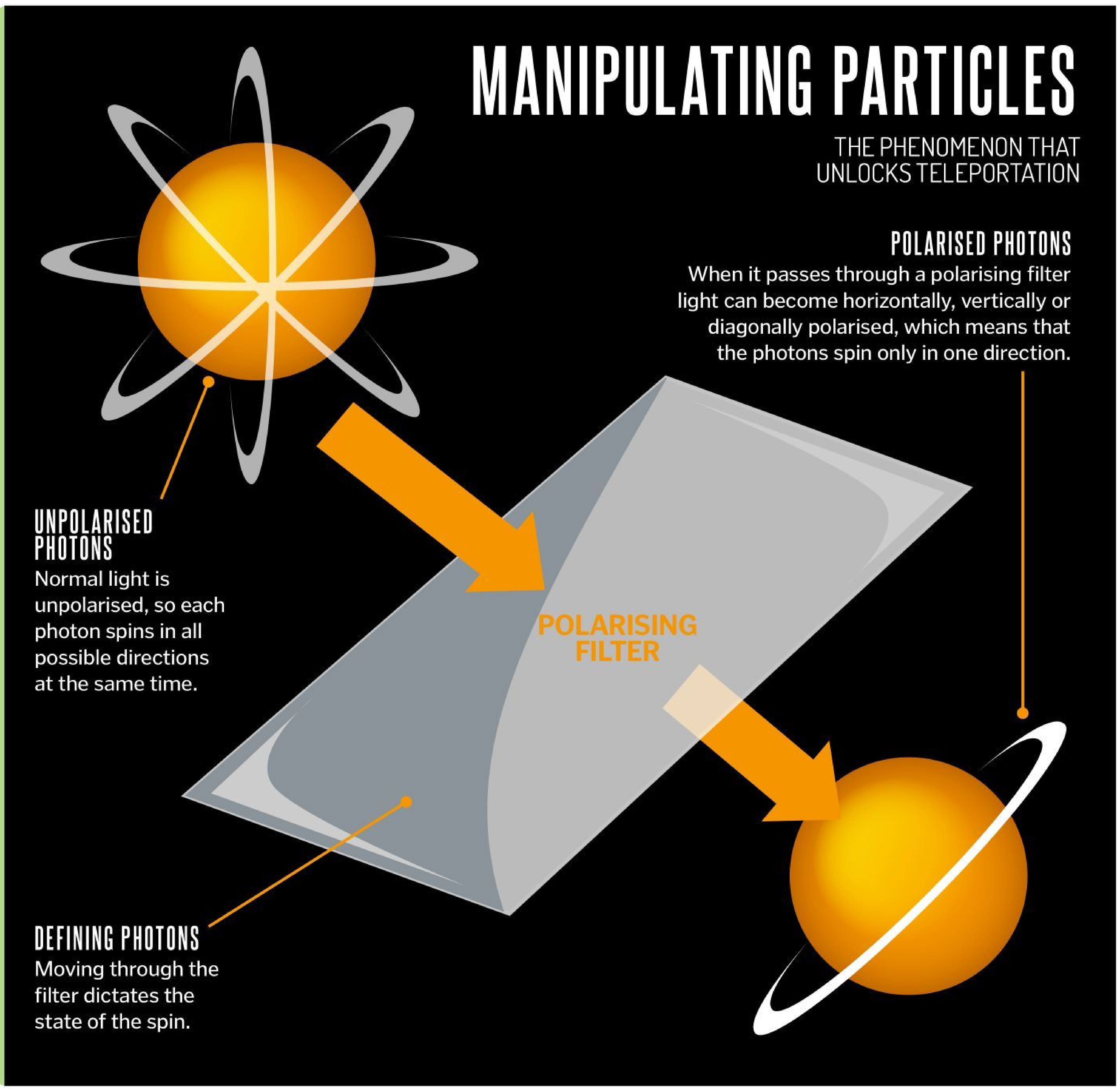
OBSERVING PHOTON ONE

When photon one is observed, superposition is lost and it will appear to be either horizontally (H) or vertically (V) polarised.

○ A scientist at the University of Geneva in Switzerland uses a laser to create entangled photons in researching quantum memory

MANIPULATING PARTICLES

THE PHENOMENON THAT UNLOCKS TELEPORTATION



POLARISED PHOTONS
When it passes through a polarising filter light can become horizontally, vertically or diagonally polarised, which means that the photons spin only in one direction.

UNPOLARISED PHOTONS
Normal light is unpolarised, so each photon spins in all possible directions at the same time.

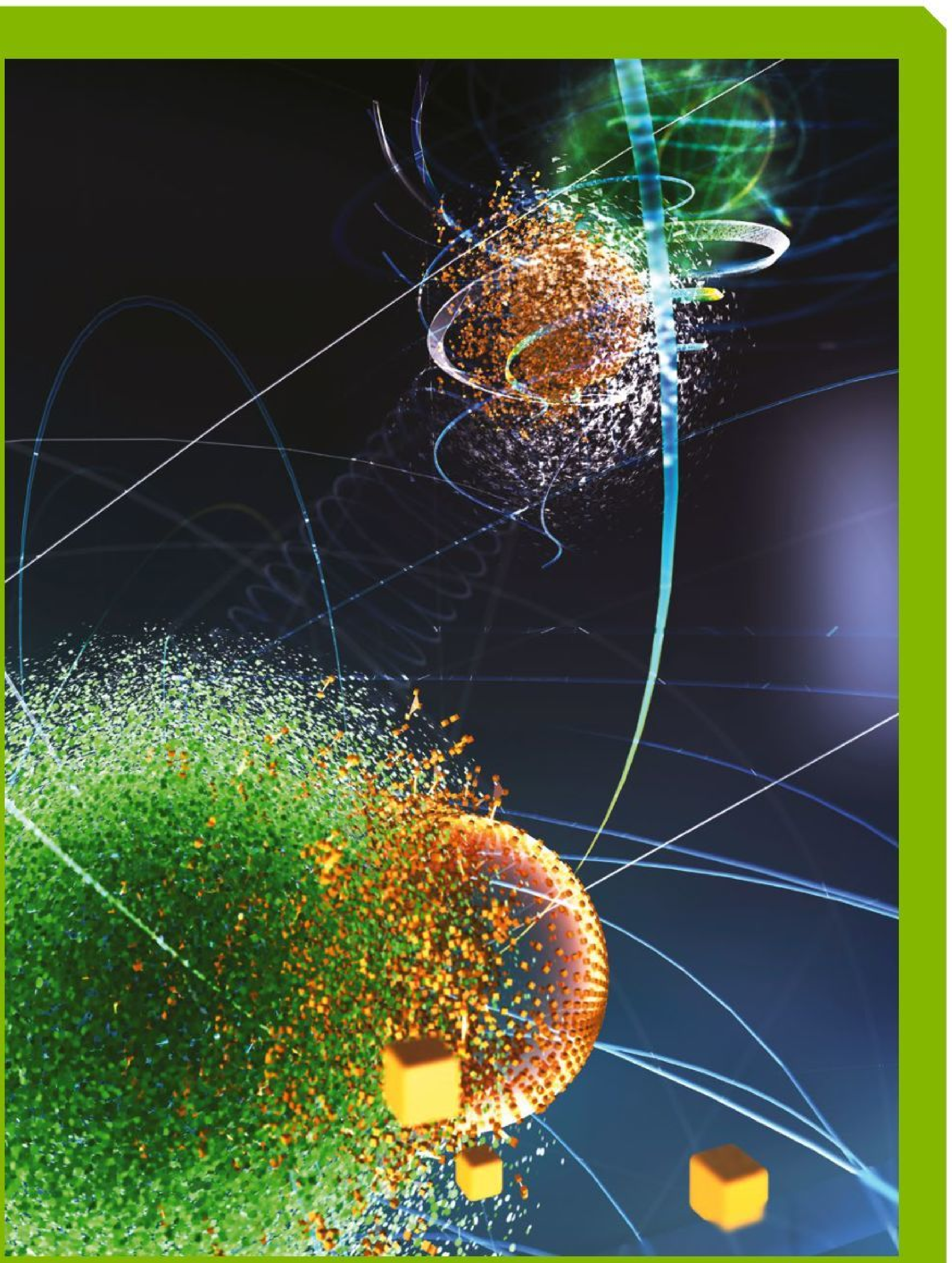
DEFINING PHOTONS
Moving through the filter dictates the state of the spin.

QUANTUM TELEPORTATION

We might be a considerable way from teleporting people, but single atoms and photons have already been teleported thanks to the use of quantum techniques.

The process involves creating two entangled particles at place A and then sending one of them to place B. Now, using clever techniques that also involve introducing a third particle that interacts with particle A, entanglement causes the particle at B to become an exact copy of the third particle. In reality, the actual particle hasn't moved, but the result is the same, so, effectively, the third particle has teleported to B's location instantly.

As with all things quantum, in practice this is incredibly difficult, and scientists are in a race to beat distance records. While the current record is 143 kilometres using a laser beam in September 2016, researchers in Calgary, Canada, and Shanghai, China, demonstrated quantum teleportation using a more practical fibre-optic network to teleport photons across their respective cities.



○ Atoms and photons can now be teleported over ever-increasing distances

states at once – a so-called state of superposition. You'll never be able to observe this odd state of affairs because, as soon as you try to do so, that object will appear to be in just the one place or one state. However, scientists have conducted cunningly devised experiments that have confirmed that this peculiar behaviour really does happen, despite indications to the contrary whenever we try to observe it.

Another strange effect is called quantum mechanical tunnelling, and it refers to the fact that a tiny object is capable of passing straight through a solid barrier without damaging it. So, for example, if you fire an electron at a sheet of gold foil, there's a possibility that it could appear at the other side with the foil still intact.

The fact that particles can be in two places at once, and that they can pass through solid objects, both stem from the dual nature of tiny objects. At one time light was thought of as a wave, but later it was discovered that it could be described as a stream of particles called photons. Conversely, electrons were once considered as miniature particles that orbited an atom's nucleus like planets orbiting a sun, but subsequently it was discovered that they could be described as wave functions.

In reality, electrons and photons each have the properties of both particles and waves, or, in other words, both concepts are correct. So that strange phenomenon in which an electron can be in two places at once is a consequence of the wave nature of electrons.

Instead of that now outdated view of orbiting electrons, wave theory concerns a so-called probability function. In other words, it describes the probability of the electron being at any particular point in space and, until the electron is observed, its position can be thought of as all points in space, albeit with some places being more likely than others.

What we've seen so far has been known since the early 20th century, and it's strange enough. So any hope of ordinary people understanding the more recent developments in quantum theory is a forlorn one. However, to illustrate just how bizarre current thinking can be, let's think briefly about the multiverse theory, although even this dates back to the 1960s and 1970s.

You'll recall that observing a particle in a state of superposition causes its previously unknown position or state to become fixed. In the science-fiction-sounding multiverse theory, as soon as

> *"Scientists have now taken their first steps in quantum teleportation"*

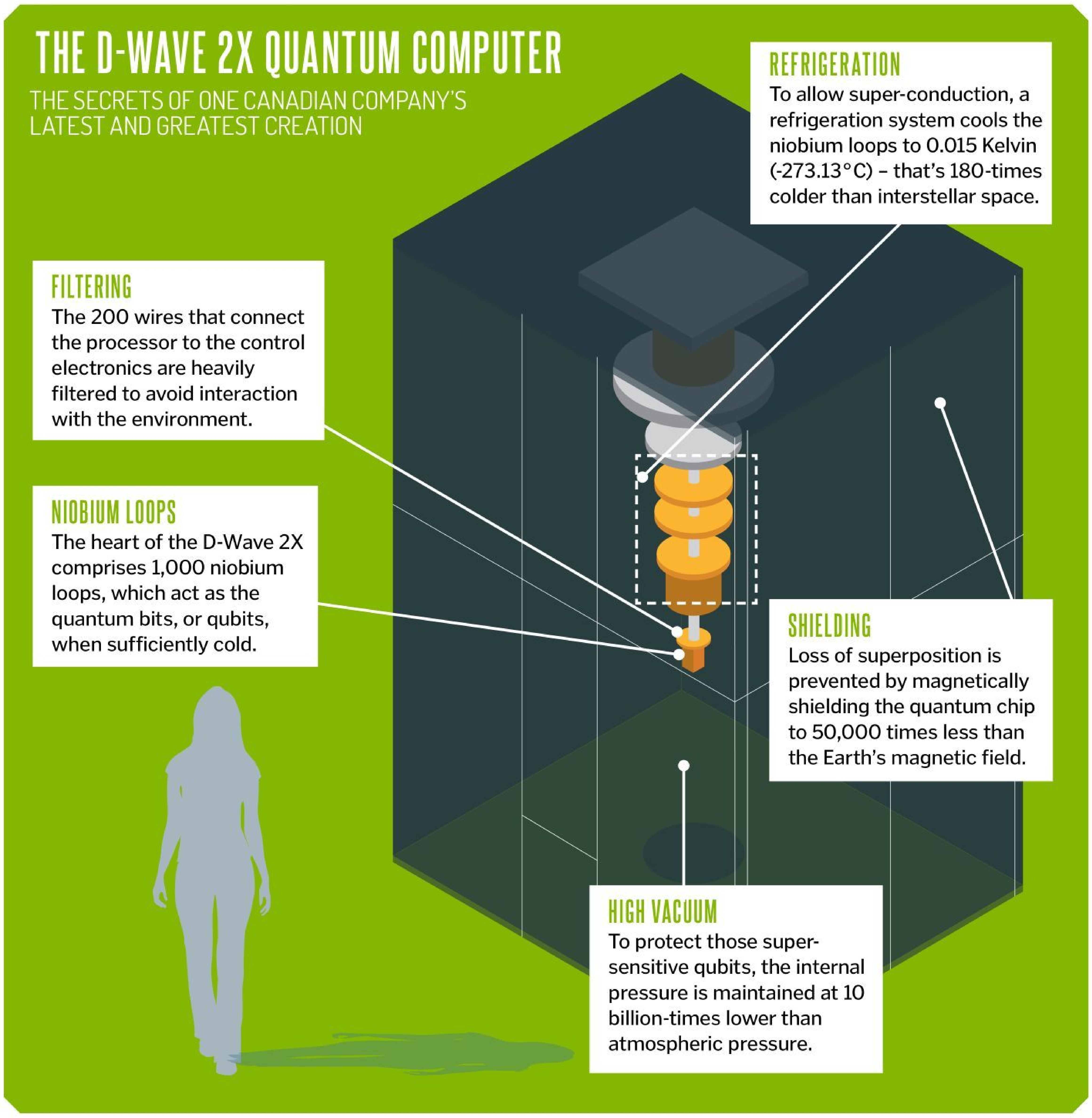
© SPL

that observation takes place, the universe splits into two or more parallel universes, with that particle being in a different location or state in each version of reality. What's more, with vast numbers of these splits taking place each second, that soon gives us an unimaginable number of parallel universes. This theory has gained additional credence recently as scientists have started to consider quantum computers. As we'll see later, compared to today's devices, if large-scale quantum computers ever become a reality, the performance they will offer will be absolutely astonishing.

This has led some scientists to suggest that there isn't enough material in the observable universe to carry out such a phenomenal number of computations. In the multiverse theory, however, that work is effectively farmed out into all of those parallel universes.

Given its very theoretical foundations, some people might be excused for thinking that quantum mechanics is an entertaining curiosity for scientists but of absolutely no practical use. But experience has proven that most theoretical studies impact the real world eventually, and there's every indication that the same is true of studies in the quantum realm. Quantum mechanics has already given birth to many technological breakthroughs, and there are tantalising glimpses of what may lie ahead.

For a start, today's solid-state devices, which impact so much of 21st-century life, depend on quantum effects. Most importantly, perhaps, is the transistor, which is the fundamental building block of computers, smartphones and



THE D-WAVE 2X QUANTUM COMPUTER

THE SECRETS OF ONE CANADIAN COMPANY'S LATEST AND GREATEST CREATION

REFRIGERATION
To allow super-conduction, a refrigeration system cools the niobium loops to 0.015 Kelvin (-273.13°C) – that's 180-times colder than interstellar space.

FILTERING
The 200 wires that connect the processor to the control electronics are heavily filtered to avoid interaction with the environment.

NIOBIUM LOOPS
The heart of the D-Wave 2X comprises 1,000 niobium loops, which act as the quantum bits, or qubits, when sufficiently cold.

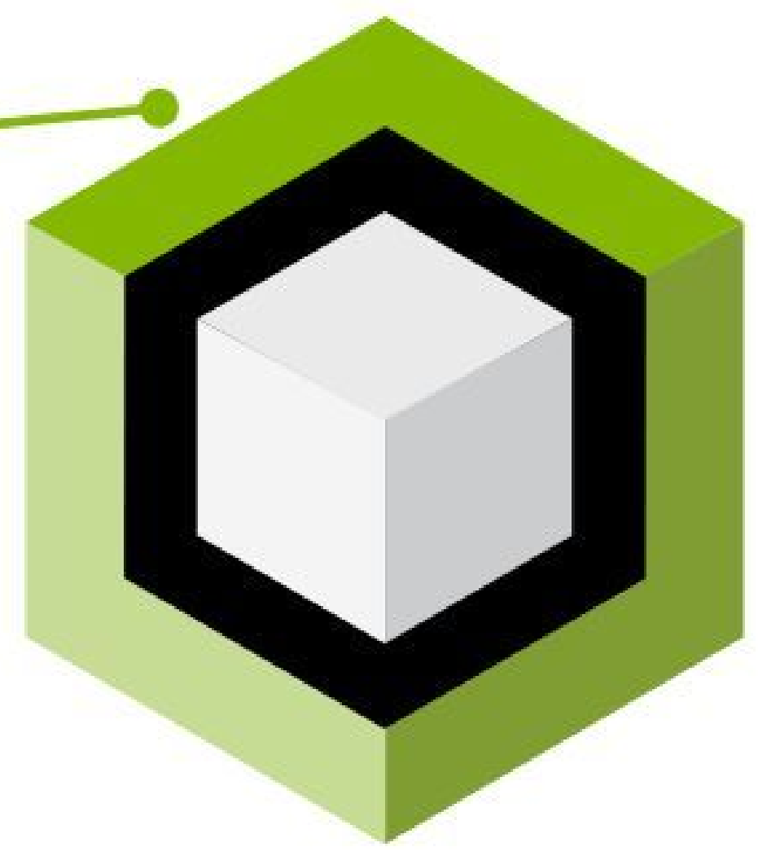
SHIELDING
Loss of superposition is prevented by magnetically shielding the quantum chip to 50,000 times less than the Earth's magnetic field.

HIGH VACUUM
To protect those super-sensitive qubits, the internal pressure is maintained at 10 billion-times lower than atmospheric pressure.

> *"A universal quantum computer would offer the ultimate in massively parallel processing"*

THE THREE TYPES OF QUANTUM COMPUTER

IBM RESEARCH HAVE IDENTIFIED THREE TYPES OF QUANTUM COMPUTER OF INCREASING DIFFICULTY BUT ALSO INCREASING POWER



QUANTUM ANNEALER
Today's only commercial quantum computer is a quantum annealer. This is a specialised architecture that is designed for a whole range of applications that are described as 'optimisation tasks'.

DIFFICULTY LEVEL
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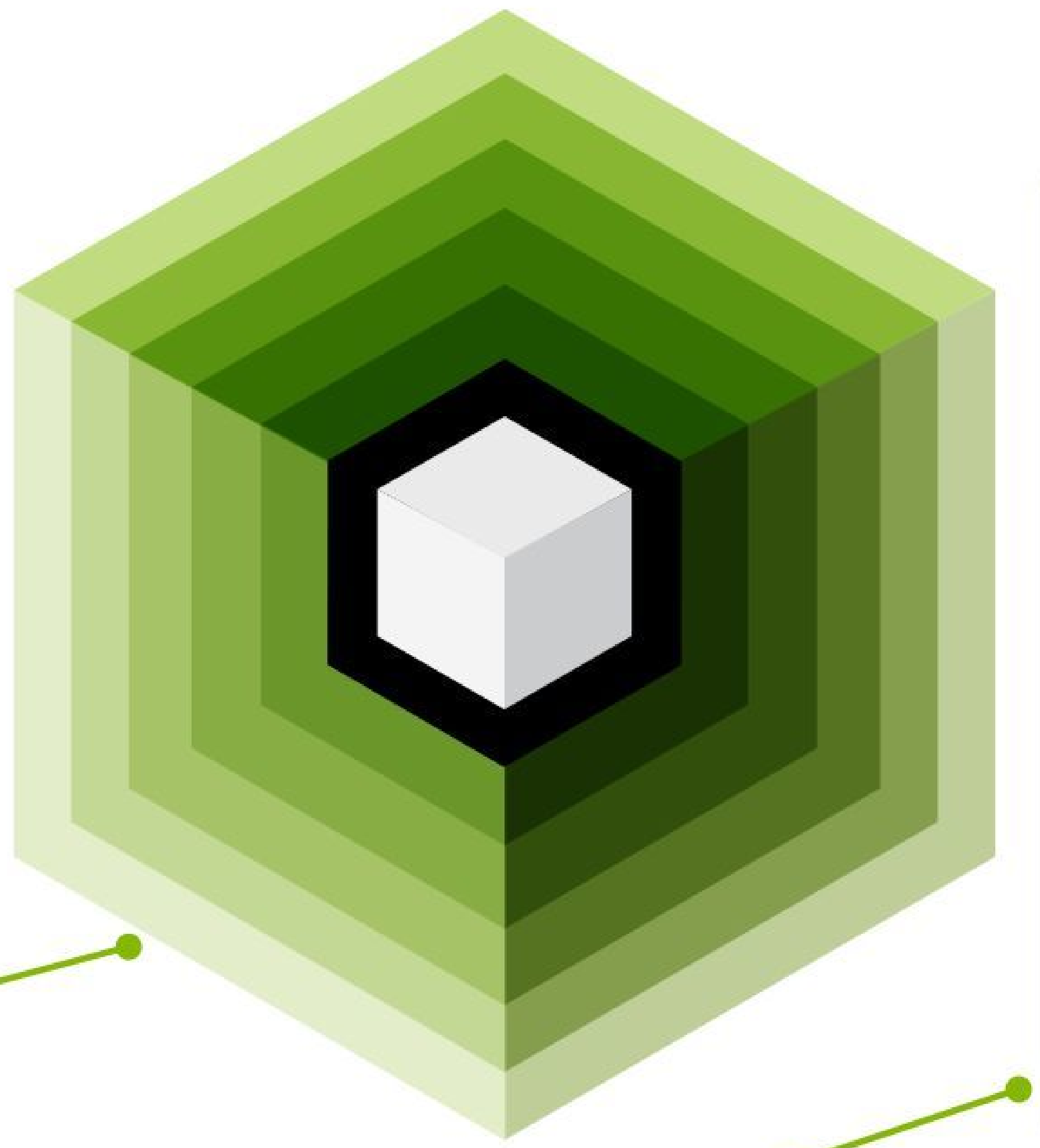

ANALOGUE QUANTUM
Before digital computers were fast enough, high-speed scientific calculations were performed using analogue computers. In the same way, quantum analogue computers could provide an interim solution until universal machines appear.

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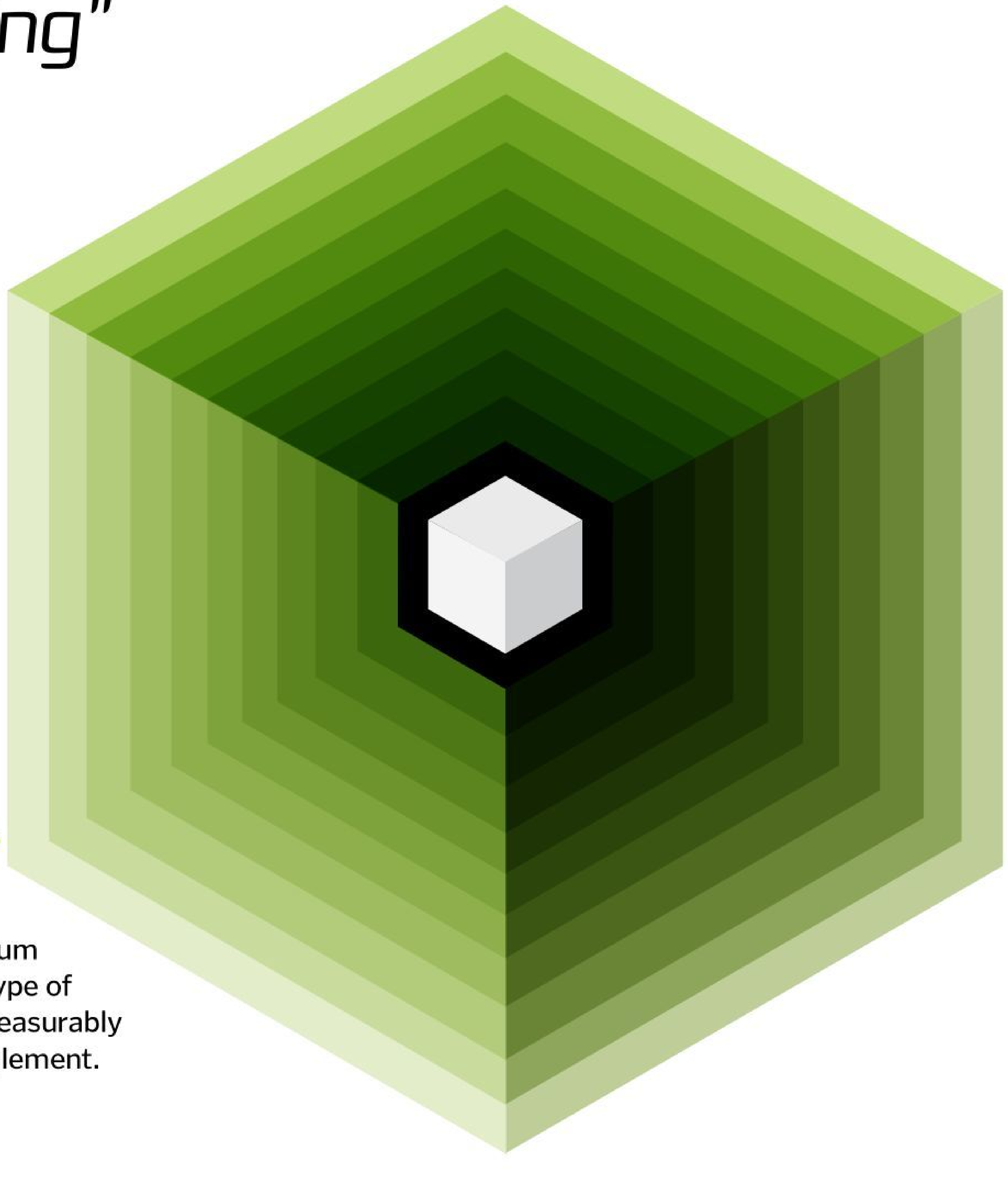

UNIVERSAL QUANTUM
Like today's computers, a universal quantum computer would be able to perform any type of computation, but it would be almost immeasurably faster thanks to superposition and entanglement.

DIFFICULTY LEVEL
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pretty much all electronic devices. Another important solid-state device is the LED and the closely related solid-state laser. The former is now revolutionising lighting by bringing hitherto unprecedented levels of energy efficiency, while the latter is key to the fibre optic cables that span the globe empowering the internet and is also a vital component in CD and DVD drives.

Atomic clocks are also reliant on quantum mechanics, and these instruments provide the precision timing needed for the operation of GPS systems on which sat navs and smartphone navigation apps rely. Quantum mechanics also underlie the principles of magnetic resonance imaging (MRI) machines, which allow physicians to see inside the body.

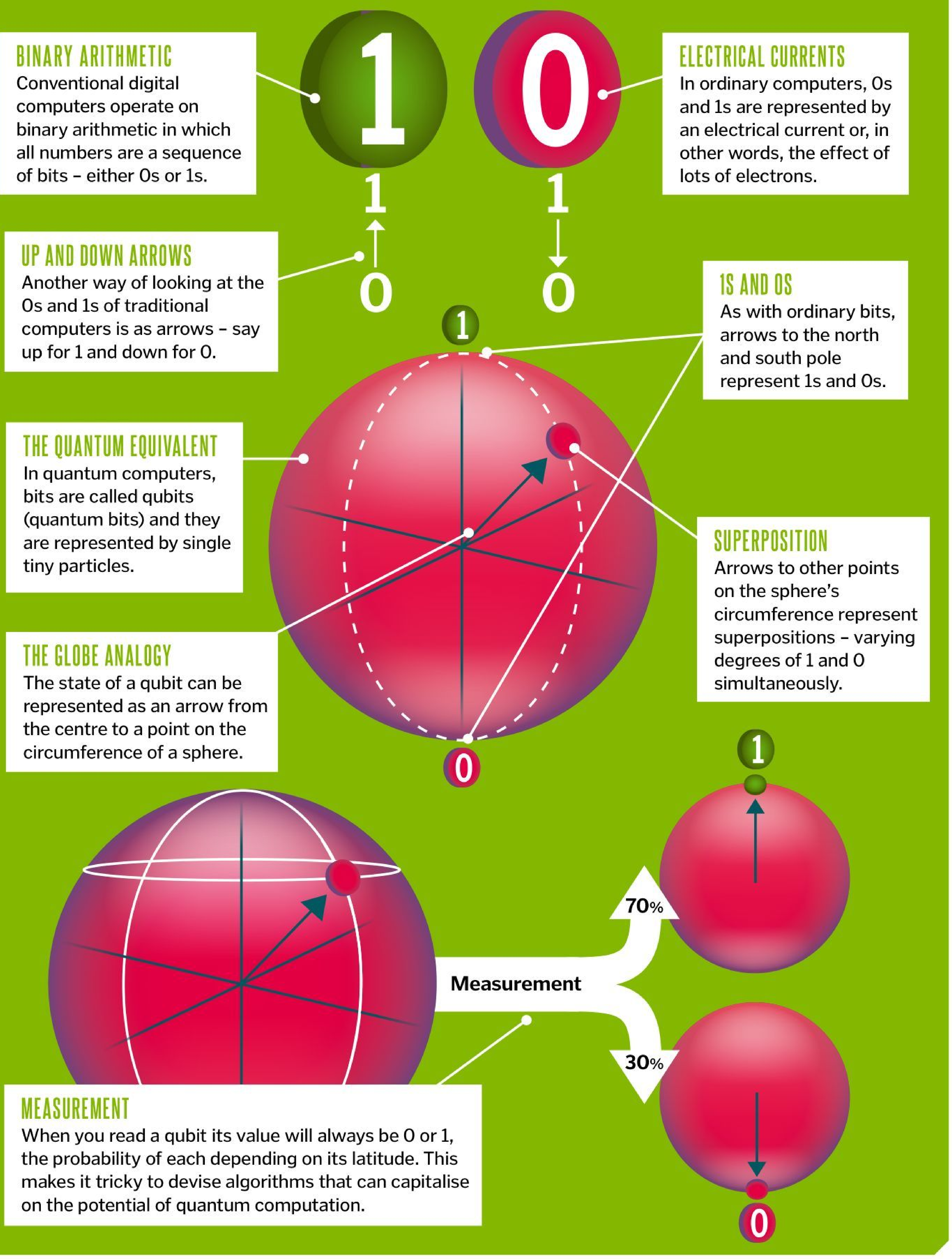
Little was said about their quantum heritage when these various technologies were developed, but we're now starting to hear about several new technologies that are much more up front about their quantum roots. What's more, these up-and-coming applications of quantum mechanics are absolutely mind blowing.

Thought that *Star Trek* style teleportation was the result of an over-active imagination? Think again – scientists have now taken their first steps in quantum teleportation. What about a code

○ MRI scanners work using the principles of quantum mechanics

QUBITS – THE SECRET OF QUANTUM COMPUTING

THIS PECULIAR QUANTUM EFFECT IS KEY TO QUANTUM COMPUTING AND SEVERAL OTHER QUANTUM TECHNOLOGIES



BINARY ARITHMETIC
Conventional digital computers operate on binary arithmetic in which all numbers are a sequence of bits – either 0s or 1s.

ELECTRICAL CURRENTS
In ordinary computers, 0s and 1s are represented by an electrical current or, in other words, the effect of lots of electrons.

UP AND DOWN ARROWS
Another way of looking at the 0s and 1s of traditional computers is as arrows – say up for 1 and down for 0.

1S AND 0S
As with ordinary bits, arrows to the north and south pole represent 1s and 0s.

THE QUANTUM EQUIVALENT
In quantum computers, bits are called qubits (quantum bits) and they are represented by single tiny particles.

SUPERPOSITION
Arrows to other points on the sphere's circumference represent superpositions – varying degrees of 1 and 0 simultaneously.

THE GLOBE ANALOGY
The state of a qubit can be represented as an arrow from the centre to a point on the circumference of a sphere.

MEASUREMENT
When you read a qubit its value will always be 0 or 1, the probability of each depending on its latitude. This makes it tricky to devise algorithms that can capitalise on the potential of quantum computation.

QUANTUM COMPUTERS BY NUMBERS

100 million times
How much faster the D-Wave 2X is compared to an ordinary computer

2^1,000
Number of solutions the current D-Wave 2X quantum computer can search simultaneously

1,000
The greatest number of entangled qubits achieved

18.4 billion billion
How many calculations a universal 64-qubit quantum computer could do simultaneously

2^16
How many simultaneous searches the first 16-qubit D-Wave quantum computer could perform in 2007

100,000
Number of qubits needed for a practical universal quantum computer

© Illustration by Neo Phoenix; Thinkstock

that is totally unbreakable? Experience tells us that however sophisticated a code, all it takes is a sufficiently powerful computer and encrypted messages can be accessed. Not so with quantum cryptography. This isn't a code that's so fiendishly difficult that it would take all the computers on the planet years to crack. This is a method of encryption that, according to the laws of quantum mechanics, is totally secure, however much computing power you throw at it. And then we have quantum computers and the world of opportunities it opens up.

For now, though, let's just say that one company is already selling a rather specialised quantum computer, and research continues into a quantum equivalent of today's PCs, a universal quantum computer. If these ever come to fruition, they won't just be incrementally faster than their predecessors, which have doubled in speed every couple of years. Instead, a truly universal quantum computer holds the promise of almost unlimited performance thanks to that strange quantum effect of superposition, coupled with the effect of entanglement.

By being in millions upon billions of states at the same time, a universal quantum computer would offer the ultimate in massively parallel processing, in which multiple operations are carried out simultaneously.

It is widely acknowledged that last century was the era of electronics. Within a period of just 52 years the very first electronic device, the vacuum tube, or valve, was invented, and this was then superseded first by the transistor and then by the integrated circuit. It then only took another 13 years for the first microprocessor to be released publicly.

Renowned German-Austrian quantum physicist Professor Rainer Blatt has described the technological developments of the last century as the first quantum revolution, and with some justification. After all, many of the developments that underpin today's society resulted from an understanding of quantum mechanics and, in particular, wave-particle duality. Professor Blatt suggests that humanity now stands at the dawn of a second quantum revolution, one that will be empowered by the weird quantum effect of entanglement.

According to Professor Blatt, "In the early 1960s, the laser was still seen as a solution to an unknown problem, and today, just over 50 years later, lasers have become an indispensable part of our lives – I expect quantum technologies to develop along similar lines."

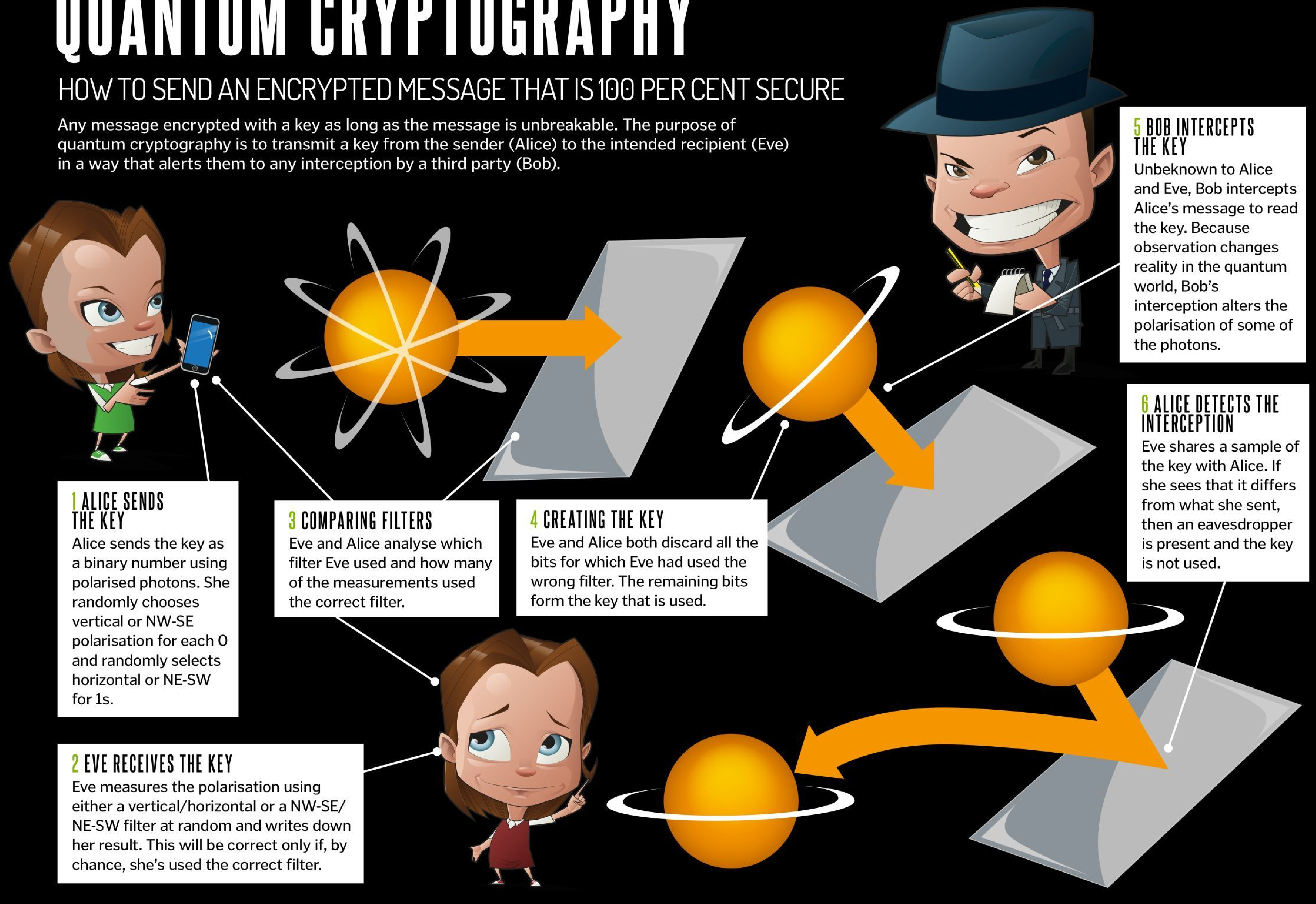
> *"We now stand at the dawn of a second quantum revolution"*

○ Quantum computing has a wide range of applications, from improving air-traffic control systems to creating better speech-recognition software

QUANTUM CRYPTOGRAPHY

HOW TO SEND AN ENCRYPTED MESSAGE THAT IS 100 PER CENT SECURE

Any message encrypted with a key as long as the message is unbreakable. The purpose of quantum cryptography is to transmit a key from the sender (Alice) to the intended recipient (Eve) in a way that alerts them to any interception by a third party (Bob).



1 ALICE SENDS THE KEY
Alice sends the key as a binary number using polarised photons. She randomly chooses vertical or NW-SE polarisation for each 0 and randomly selects horizontal or NE-SW for 1s.

2 EVE RECEIVES THE KEY
Eve measures the polarisation using either a vertical/horizontal or a NW-SE/NE-SW filter at random and writes down her result. This will be correct only if, by chance, she's used the correct filter.

3 COMPARING FILTERS
Eve and Alice analyse which filter Eve used and how many of the measurements used the correct filter.

4 CREATING THE KEY
Eve and Alice both discard all the bits for which Eve had used the wrong filter. The remaining bits form the key that is used.

5 BOB INTERCEPTS THE KEY
Unbeknown to Alice and Eve, Bob intercepts Alice's message to read the key. Because observation changes reality in the quantum world, Bob's interception alters the polarisation of some of the photons.

6 ALICE DETECTS THE INTERCEPTION
Eve shares a sample of the key with Alice. If she sees that it differs from what she sent, then an eavesdropper is present and the key is not used.

APPLYING QUANTUM MECHANICS

IN THE FUTURE THERE MAY BE NUMEROUS WAYS TO USE THIS RAPIDLY GROWING TECHNOLOGY

IMAGE SEARCHING

Humans are easily able to detect familiar objects such as trees, lakes and cats when they look at a photograph. Teaching computers to do likewise is a really difficult programming task because it's so hard to define the essence of 'cat-ness', for example. But machine learning tasks like this are natural applications for quantum computers. Google has already invested considerable research effort into image analysis to make online picture searching more efficient. This was demonstrated by teaching a quantum computer to recognise cars in photos, a task it was then able to do much quicker than an ordinary computer could ever achieve.

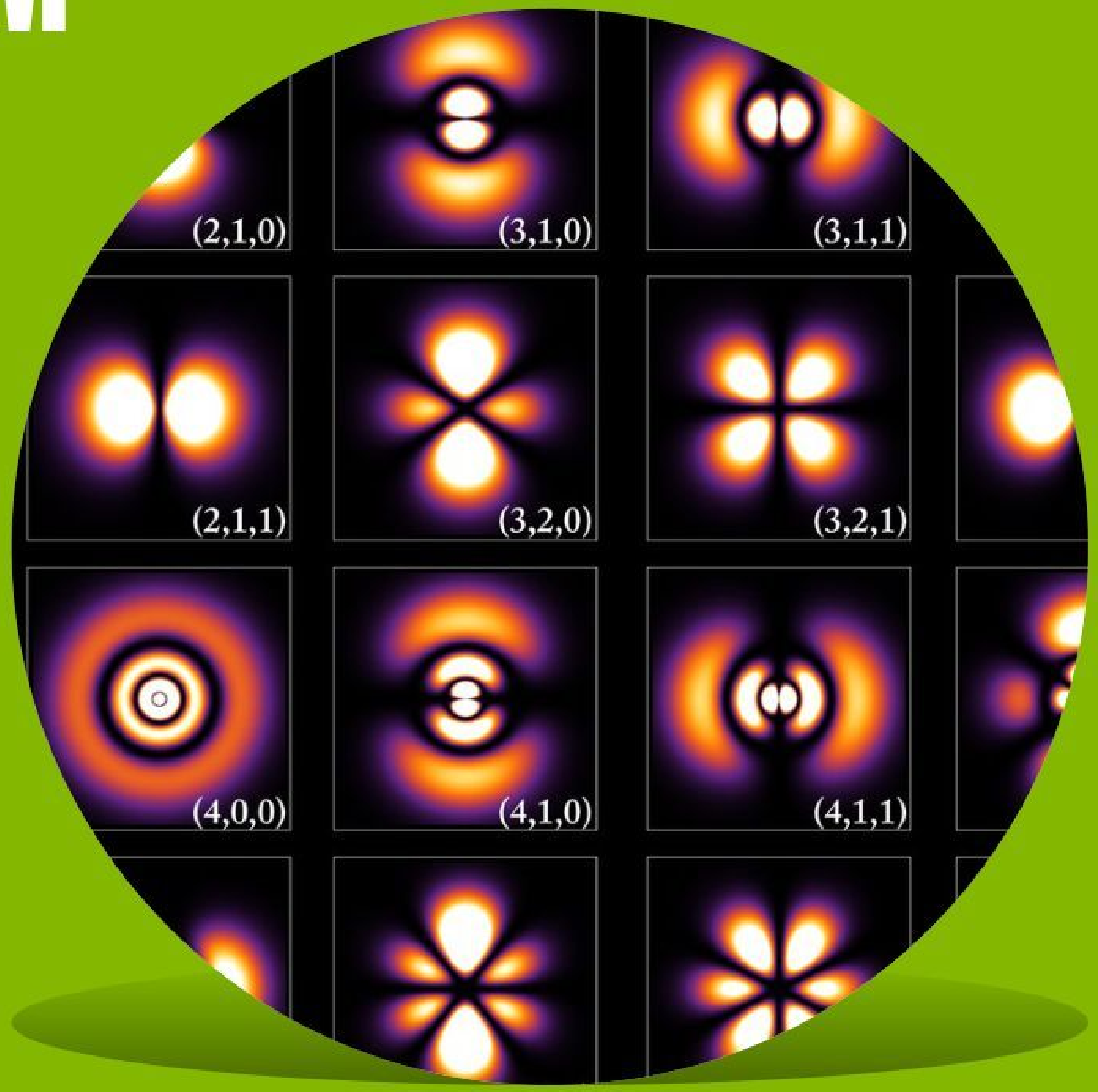
RADIOTHERAPY OPTIMISATION

According to D-Wave Systems, their D-Wave 2X computer, working with a conventional computer, will help to optimise radiotherapy. This treatment aims to target a tumour while minimising harmful exposure to the rest of the body, with several beams intersecting at the tumour. Its optimisation involves juggling thousands of variables. To achieve it, simulations would be carried out on a huge number of possibilities using a conventional computer, while a quantum annealing computer would determine the most probable scenarios for simulation.

ASTRONOMY

Given that NASA jointly owns one of the world's first quantum computers, it's hardly surprising that astronomy will probably be one of the main beneficiaries of this new model of computation. The space agency has its sights set on several ways that quantum computing can assist in the exploration of space, but many of them can be summed up as searching through huge amounts of data for the proverbial needle in the haystack. A classic example is the search for habitable exoplanets; Earth-like planets in orbit at the ideal distance from faraway stars that might just be capable of hosting life.

> *"Encrypted messages would be an open book for a general-purpose quantum computer"*



QUANTUM SIMULATION

It might seem like a circular argument but, just as an understanding of quantum mechanics has now given us quantum computers, scientists are now hoping that those same quantum computers will help them to better understand quantum systems by simulating them. Today's computers are able to carry out simulations of quantum effects but, such is the complexity of quantum systems, they are incredibly slow. It perhaps comes as no surprise, then, that computers that are based on the strange world of quantum mechanics are much more capable of simulating quantum systems and, thereby, help scientists to gain new insights.

CODE BREAKING

A universal quantum computer would be able to factor large numbers with ease, a phenomenally time-consuming job for conventional computers. Today's ciphers rely on the fact that factoring is difficult, but encrypted messages would be an open book once general-purpose quantum computers become reality. This might be useful to the military and police forces – for example, in the fight against terror and organised crime – but it would also be a boost to cyber criminals. It's quite appropriate that the same quantum technology that might make today's encryption techniques obsolete could provide a replacement in the form of quantum cryptography.

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MIRACLE SCIENCE

REVEALED: THE BREAKTHROUGHS THAT WILL SAVE YOUR LIFE

Modern medicine would seem miraculous to people living less than 100 years ago, but the advancements on the horizon are even more incredible. Scientists from a wide range of different specialisms are bringing the latest developments together to create an array of new medical technologies that could transform the way we diagnose, treat and even cure disease.

Nanotechnology is taking medical treatment down to the molecular scale, focusing on the minute machinery that keeps the body ticking over, while stem cells could provide a renewable source of replacements for every cell in the human body. Personalised medicine promises to tailor treatments to each patient's individual genetic profile, and advances in neuroscience, computing, robotics and electronics are allowing advanced prosthetics to respond directly to commands sent by the brain. Vaccinations could one day be delivered painlessly via thousands of microscopic projections, while custom combinations of vitamins or drugs could be printed into convenient daily pills.

While we of course can't be sure which of today's cutting-edge techniques will make it all the way to the medical clinics of the future, with technology progressing this rapidly, there are certain to be more medical 'miracles' just around the corner.

NANOMEDICINE

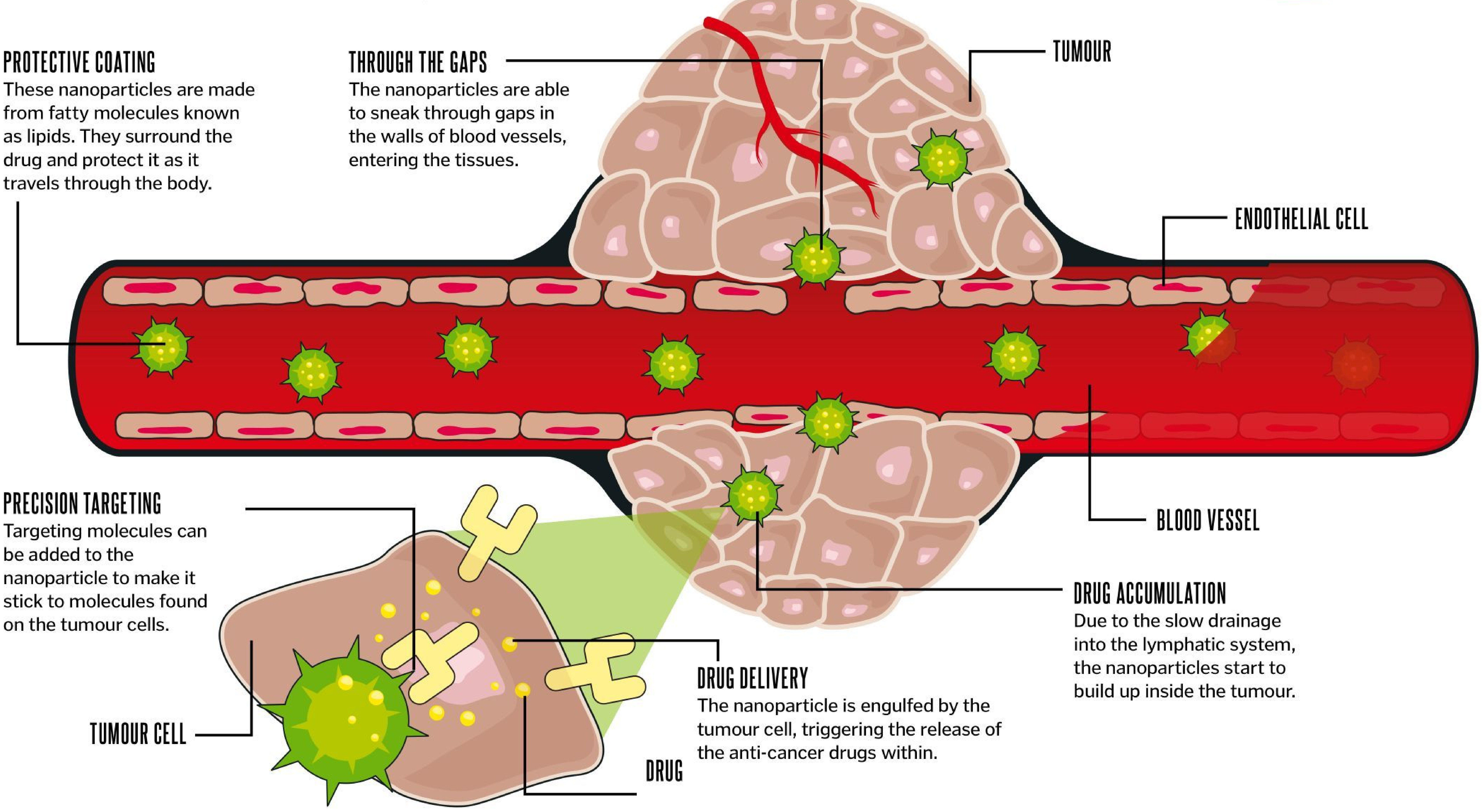
The molecular machinery that keeps the human body running is built on a nanometre scale. Haemoglobin molecules (the proteins that carry oxygen in your blood) are around five to seven nanometres in diameter – about 10,000-times narrower than a human hair!

Nanomedicine attempts to interact with this miniature world by using materials that measure less than 1,000 nanometres across. Down at this tiny scale, scientists hope to develop high-precision nanotechnology that could one day repair or replace damaged cell components.

Nanomaterials have already entered the clinic, where they are being used to make capsules that carry tiny packages of drugs into the body. Some capsules help to protect the drug from being broken down as it travels to the right part of the body, and others assist with targeting, ensuring that the treatment gets to the right place.

NANOMEDICINE IN ACTION

NANOPARTICLES MADE FROM FATTY MOLECULES CAN HELP TO GUIDE DRUGS TO THE RIGHT PART OF THE BODY, SUCH AS A TUMOUR



PROTECTIVE COATING
These nanoparticles are made from fatty molecules known as lipids. They surround the drug and protect it as it travels through the body.

THROUGH THE GAPS
The nanoparticles are able to sneak through gaps in the walls of blood vessels, entering the tissues.

PRECISION TARGETING
Targeting molecules can be added to the nanoparticle to make it stick to molecules found on the tumour cells.

DRUG DELIVERY
The nanoparticle is engulfed by the tumour cell, triggering the release of the anti-cancer drugs within.

DRUG ACCUMULATION
Due to the slow drainage into the lymphatic system, the nanoparticles start to build up inside the tumour.

DETECTING DISEASES

Inspired by the *Star Trek* Tricorder, the Qualcomm Tricorder XPRIZE offers $10 million (over £6.5 million) to a team able to design a portable medical analyser. The aim is to be able to detect 16 common diseases, such as anaemia, diabetes and tuberculosis, and to monitor five vital signs, including blood pressure, heart rate and oxygen saturation. Technology like this could make diagnosis much simpler, potentially even allowing people to monitor their own health at home.

The competition was launched in 2012, and the winner was due to be announced in 2016. While no team met all the requirements to win, finalists included the Scanadu Scout, which monitors vital signs like blood pressure when held next to the head, and the rHEALTH sensor, which can detect Ebola from a tiny drop of blood.

○ Miniature 'lab-on-chip' technology allows for portable medical testing

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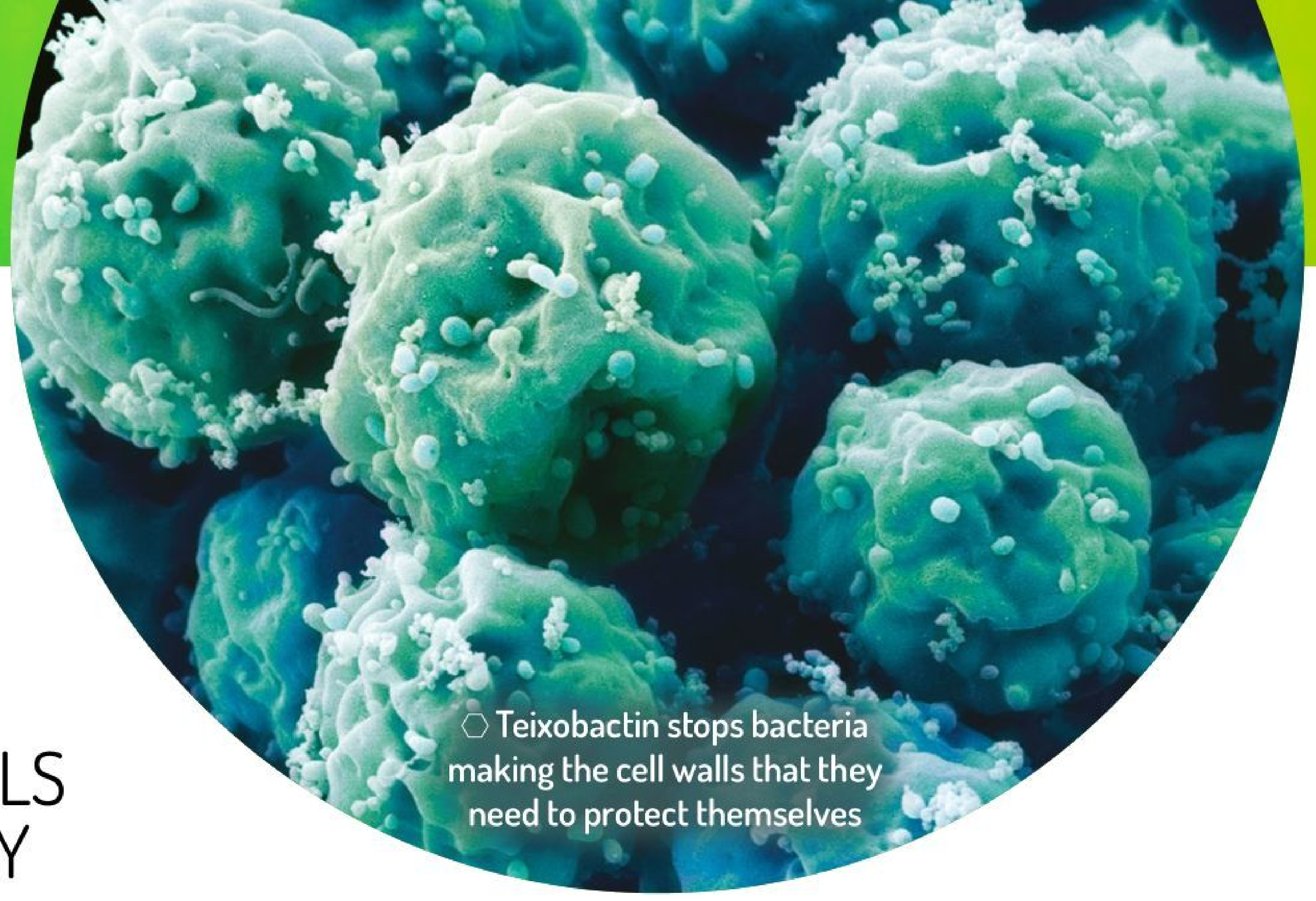
REGENERATING DAMAGED TISSUES

WITH INCREDIBLE CAPACITY FOR REGENERATION, STEM CELLS HAVE THE POTENTIAL TO REPLACE EVERY CELL IN THE BODY


Teixobactin stops bacteria making the cell walls that they need to protect themselves

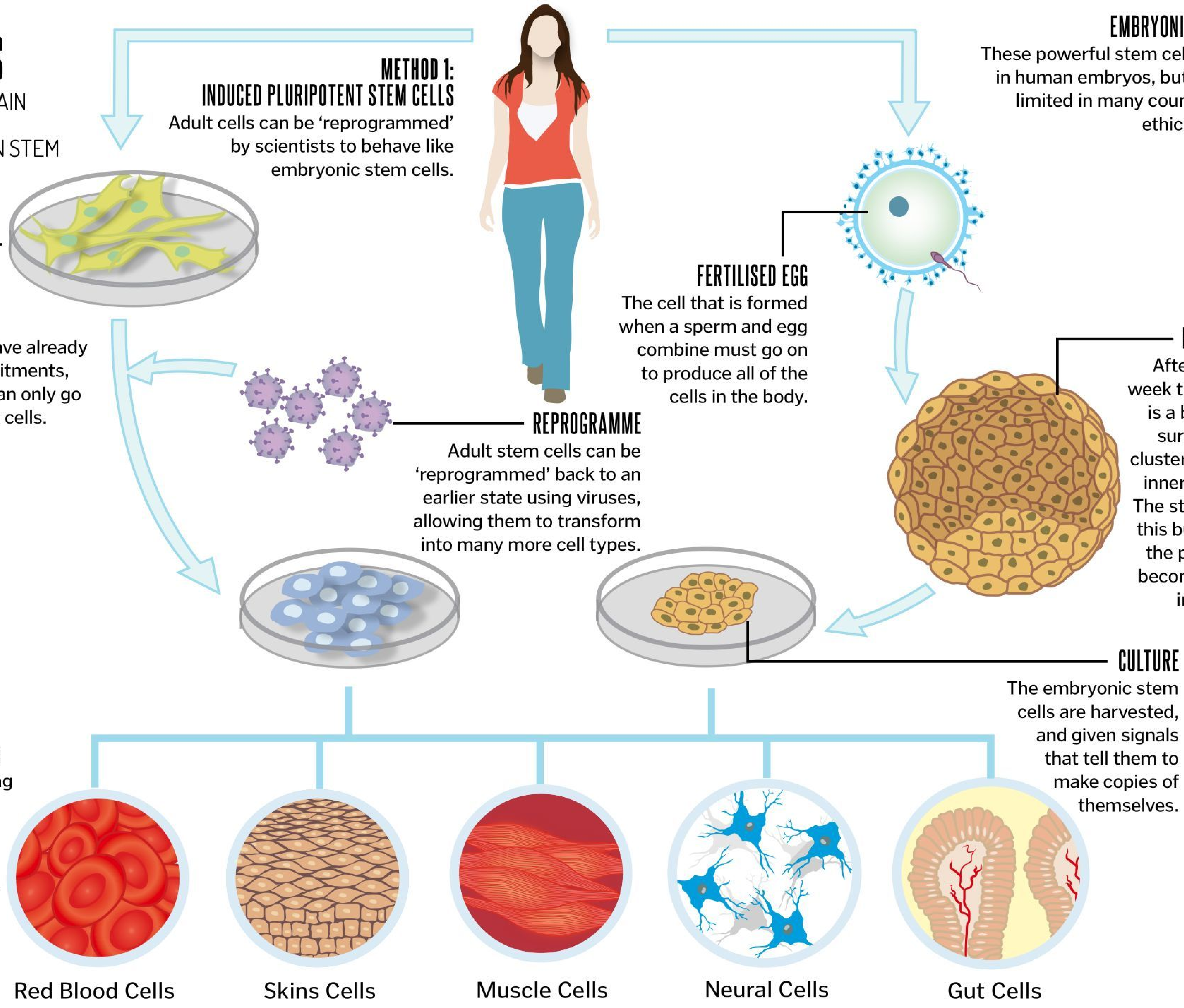
Most of the cells in your body are highly specialised; each is dedicated to its individual role, and once it has committed to becoming a certain cell type, the decision is permanent. Stem cells, however, have not yet chosen a specialism. Instead, they support growth and repair, and are able to carry on making copies of themselves long after most other adult cells would have stopped dividing. Each of those copies can rest, make more copies, or begin the process of transforming into a specialist cell.

The specialism that the stem cell chooses varies based on the signals that it receives and alo depending on the type of stem cell that it is – an embryonic stem cell, or one of the many different kinds of adult stem cell. Embryonic stem cells are the most powerful; they are found in the developing embryo and, with the right signals, can be transformed into any cell in the human body.

Given these incredible properties, it is no wonder stem cells are receiving a lot of attention. Doctors already perform stem cell transplants to replace lost bone marrow, and stem cells are used to create skin grafts. In the future it is hoped they will be used to repair damaged tissues or even to rebuild entire organs.

GROWING STEM CELLS

THERE ARE TWO MAIN APPROACHES TO PRODUCING HUMAN STEM CELLS IN THE LAB



METHOD 1: INDUCED PLURIPOTENT STEM CELLS
Adult cells can be 'reprogrammed' by scientists to behave like embryonic stem cells.

METHOD 2: EMBRYONIC STEM CELLS
These powerful stem cells are found in human embryos, but research is limited in many countries due to ethical concerns.

ADULT STEM CELLS
Adult stem cells have already made some commitments, and in this state, can only go on to make certain cells.

FERTILISED EGG
The cell that is formed when a sperm and egg combine must go on to produce all of the cells in the body.

BLASTOCYST
After around a week the embryo is a ball of cells surrounding a cluster called the inner cell mass. The stem cells in this bundle have the potential to become any cell in the body.

REPROGRAMME
Adult stem cells can be 'reprogrammed' back to an earlier state using viruses, allowing them to transform into many more cell types.

CHANGE CULTURE CONDITIONS
Stem cells can be encouraged to become different types of specialised adult cells by varying their conditions.

CULTURE
The embryonic stem cells are harvested, and given signals that tell them to make copies of themselves.

IS STEM CELL THERAPY A GOOD IDEA?

THERE ARE ARGUMENTS FOR AND AGAINST USING STEM CELLS FOR MEDICINE

ADVANTAGES

☑ Stem cells could be used to repair tissues.
☑ They could help to build entire organs for transplant.
☑ Your own stem cells would be a perfect genetic match.

DISADVANTAGES

☒ The long-term effects of using stem cells are not yet known.
☒ There are ethical concerns surrounding the use of human embryos.
☒ There are many diseases that stem cells cannot treat.

CURING BLINDNESS

COULD STEM CELLS BE USED TO RESTORE SIGHT?

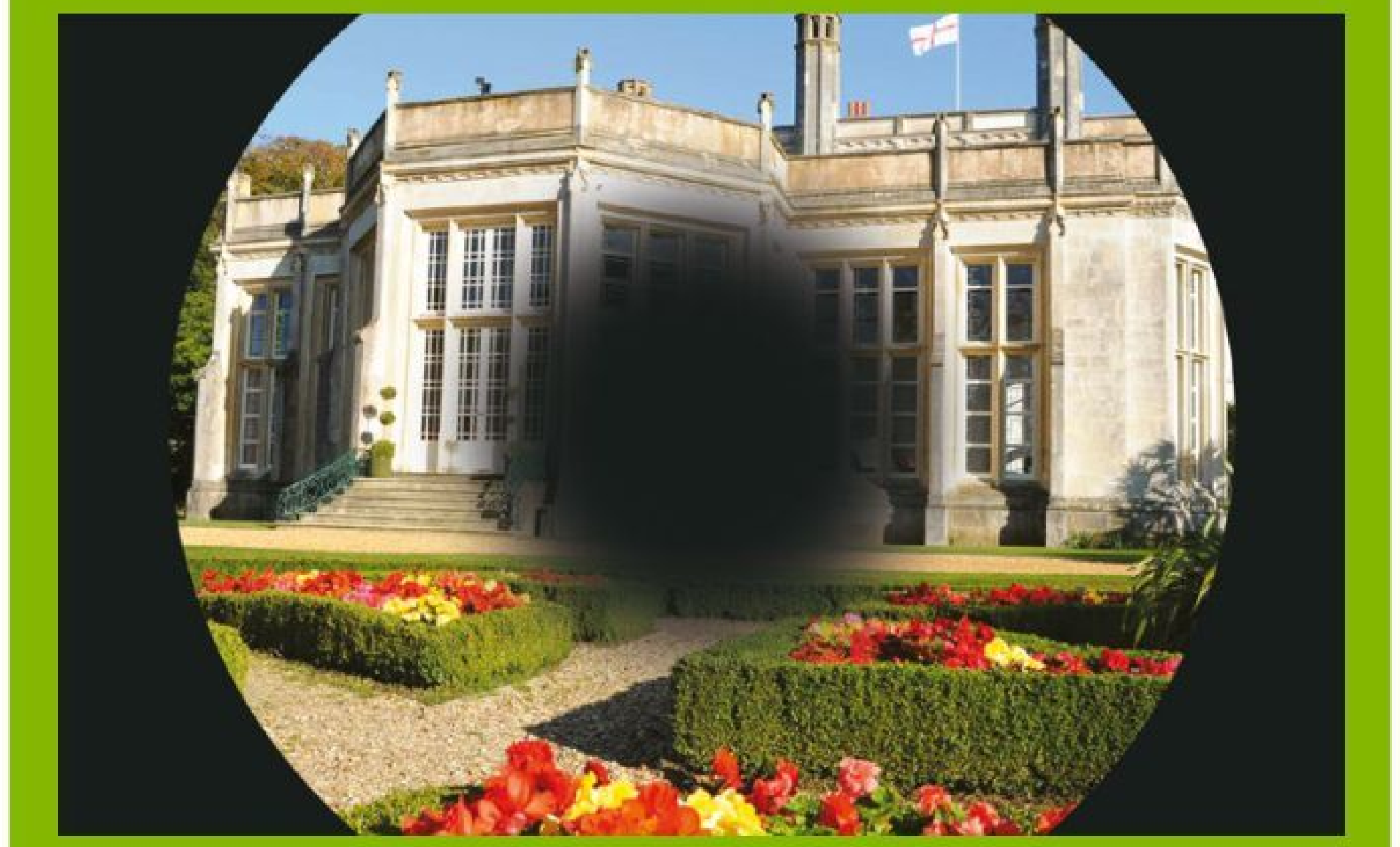
The London Project to Cure Blindness is a collaboration between Moorfields Eye Hospital, University College London, the University of Sheffield, the British Government and pharmaceutical company Pfizer. It aims to tackle a disease called 'wet age-related macular degeneration' (wet AMD), which causes rapid loss of central vision.

The team are using stem cells to grow sheets of retinal pigment epithelium (RPE) cells. These cells form a brown-coloured layer on the back of the eye that helps to absorb scattered light, aiding with vision, and they help to nourish and protect the rods and cones that detect light. The RPE cell layer can become damaged in wet AMD, so the team have used stem cells to grow a patch of new RPE cells to replace them.

The new cells behave just like the real thing in the lab,and in 2015 the first patient received the new treatment as part of a clinical trial. A further nine patients have since been tested to find out whether this pioneering treatment is safe, and crucially, whether it works. Excitingly, the patients have reported a return of their central vision. In the future, the team hope to be able to use stem cells to grow new rod and cone cells, repairing damage to the light-sensing machinery of the eye.

WHAT IS AGE-RELATED MACULAR DEGENERATION?

Age-related macular degeneration (AMD) is the leading cause of sight loss in adults in the UK, affecting over 500,000 people. The most common type is 'dry' AMD, caused by the breakdown of light-sensitive cells at the back of the eye, but people can also have more aggressive 'wet' AMD, caused by abnormal blood vessel formation. Both lead to a loss of central vision.

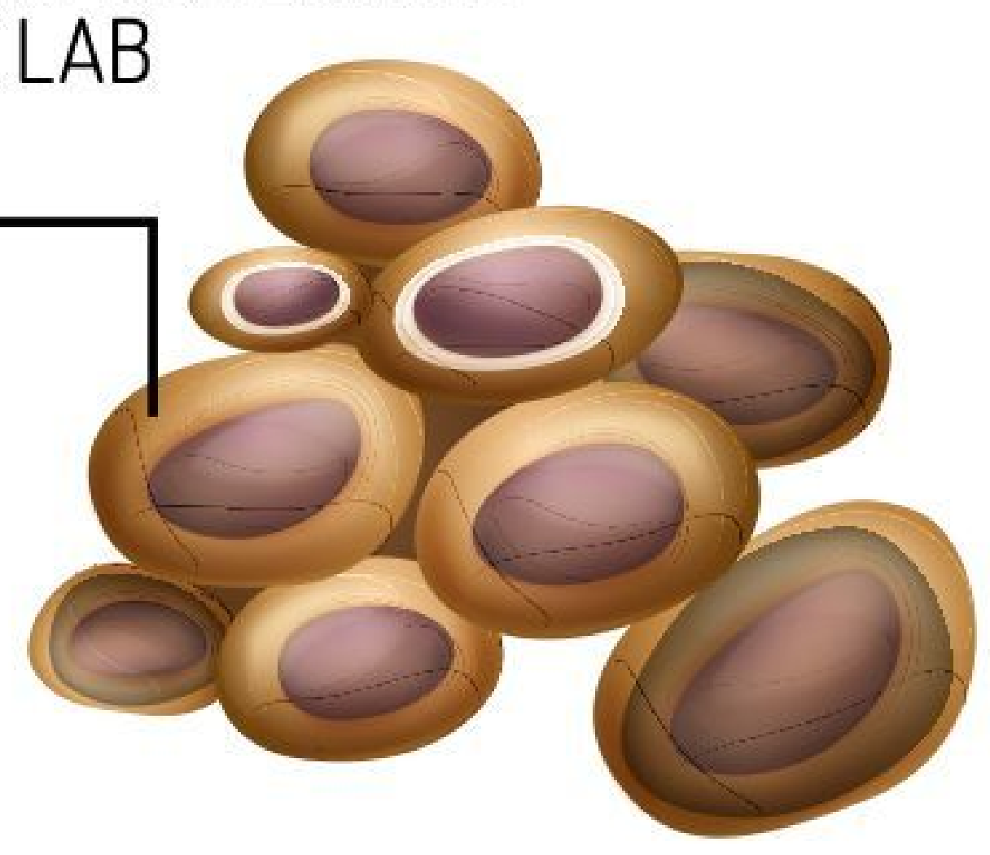


○ AMD doesn't cause complete blindness but affects the central vision, leaving only the edges intact

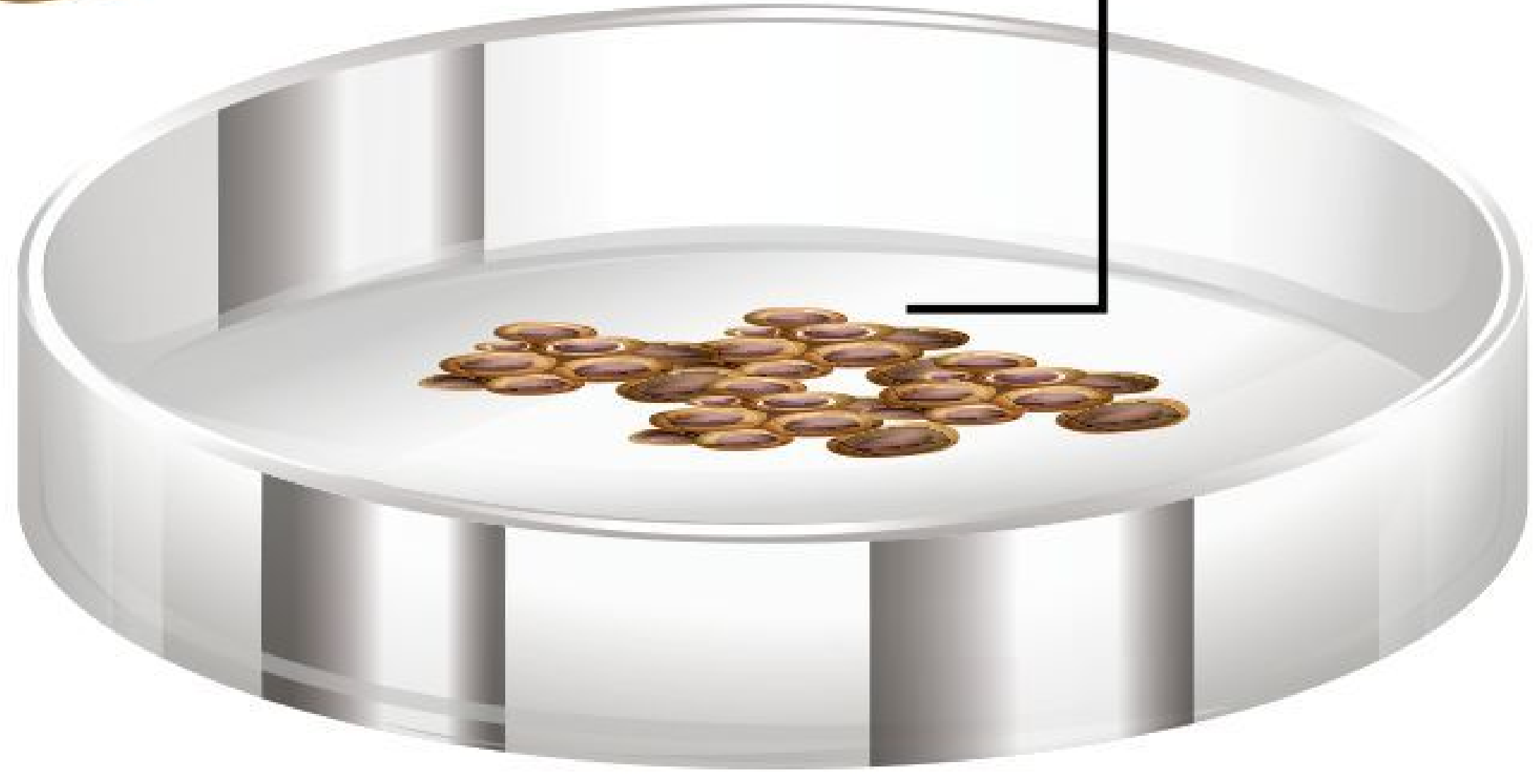
THE TREATMENT PROCESS

HOW STEM CELLS CAN BE TRANSFORMED INTO SPECIALISED EYE CELLS IN THE LAB

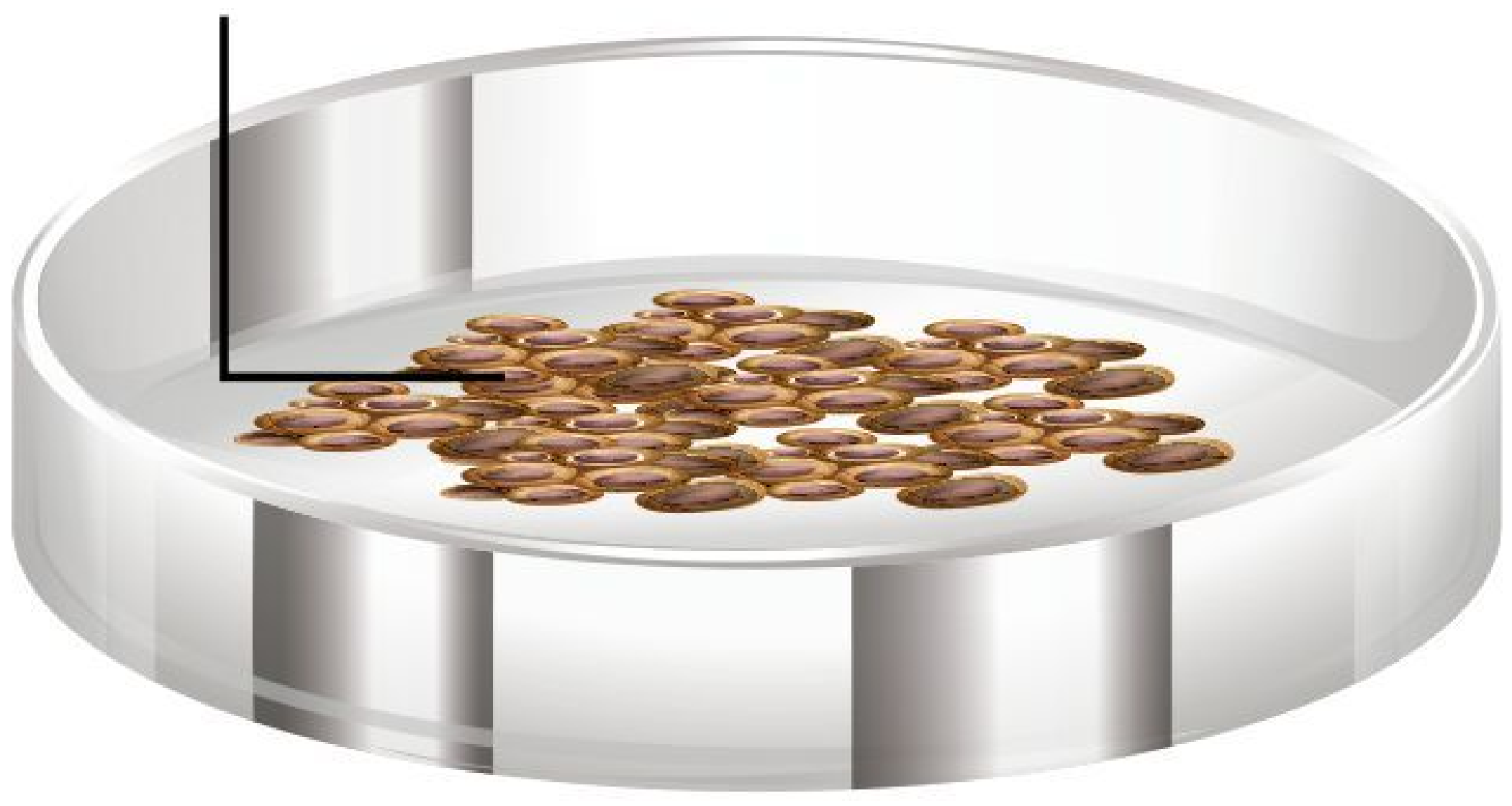
1 COLLECT STEM CELLS
Stem cells are able to make copies of themselves indefinitely and are capable of transforming into any cell in the human body, making them the perfect tool for repairing damaged tissues.

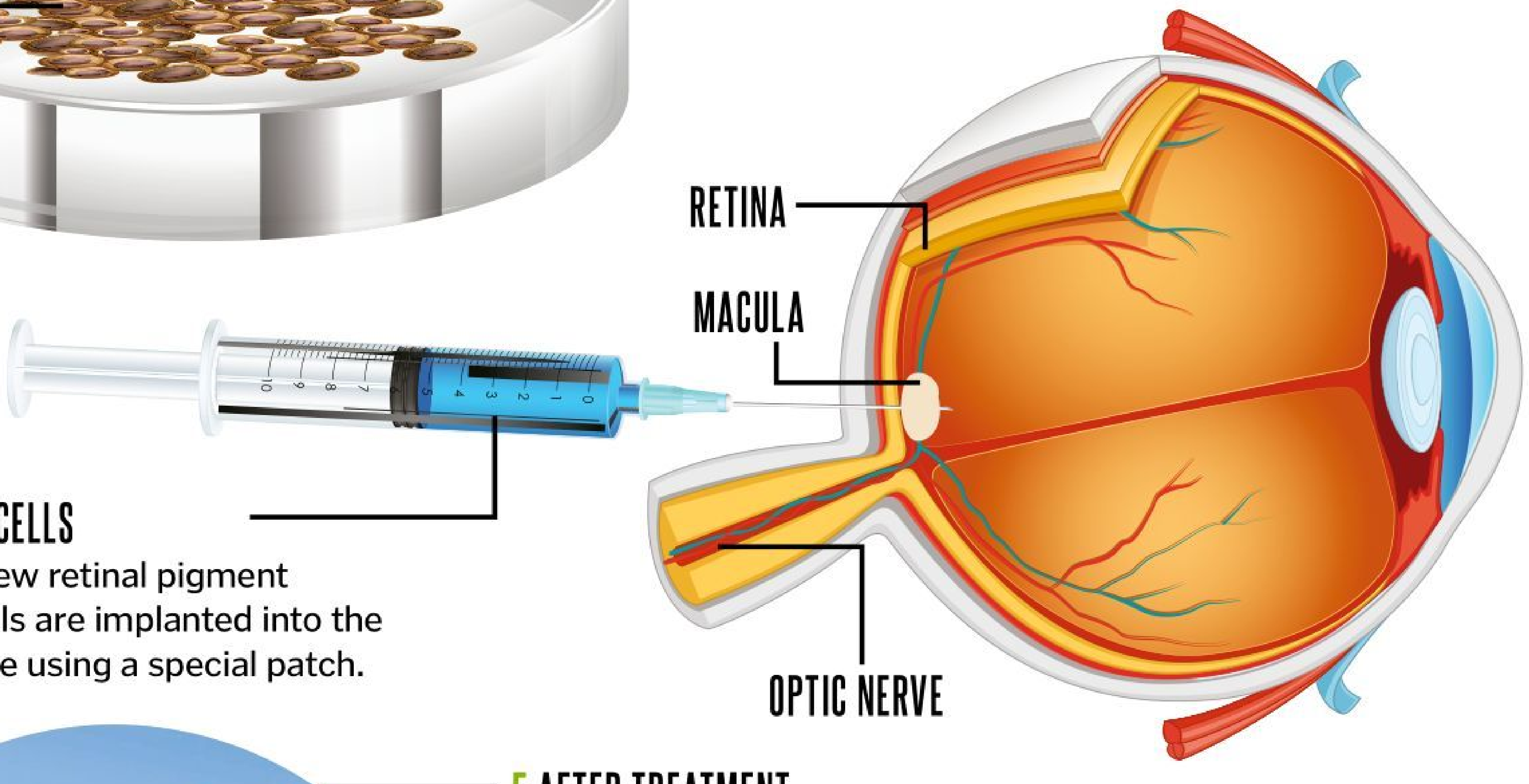


2 ADD GROWTH FACTORS
The stem cells are given chemicals called growth factors, which encourage them to divide over and over to produce hundreds of identical clones.



3 ADD DIFFERENTIATION FACTORS
Researchers can control what type of cell the stem cells will become by using different combinations of chemicals. This process is known as differentiation.





4 IMPLANT THE CELLS
The layer of new retinal pigment epithelium cells are implanted into the back of the eye using a special patch.

5 AFTER TREATMENT
It is hoped that this treatment will help to restore some central vision to patients with age-related macular degeneration.

> *"The specialism that the stem cell chooses varies based on the signals it receives"*

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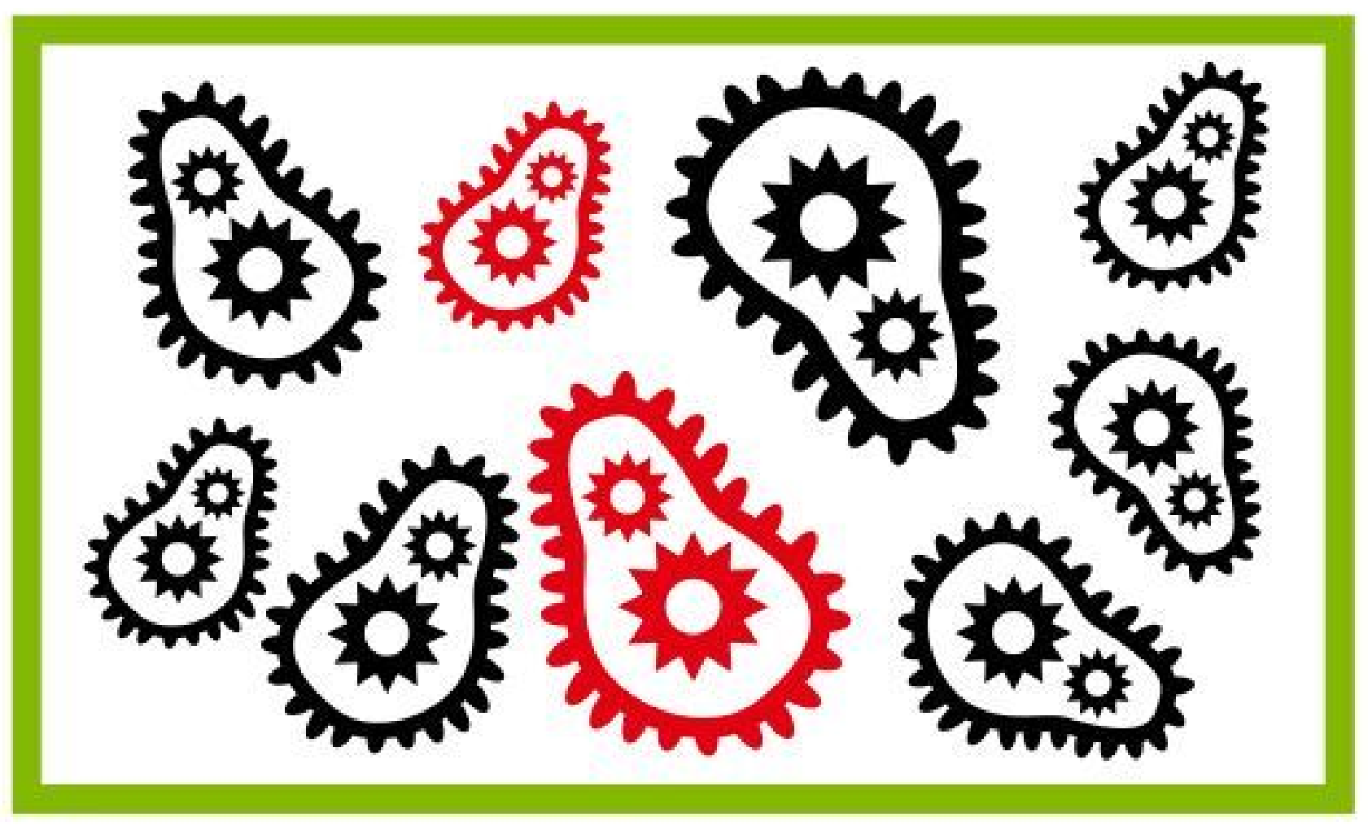
DEFEATING SUPERBUGS

IF WE ARE GOING TO SURVIVE FUTURE INFECTIONS, WE NEED TO TACKLE ANTIBIOTIC RESISTANCE

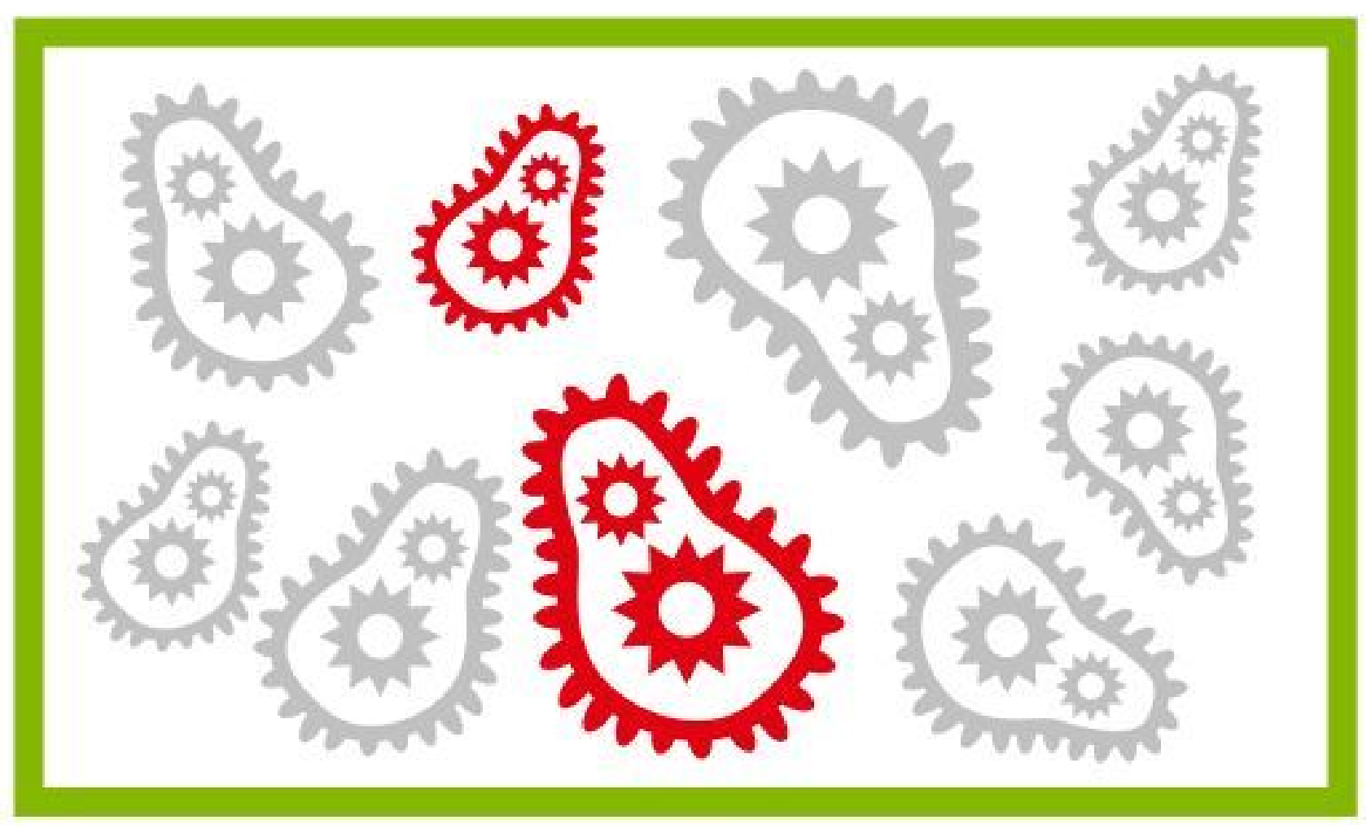
Just like humans, bacteria have variations in their genes that give them slightly different characteristics. This means that some bacteria will succumb to antibiotics faster than others. If the more hardy bacteria survive until the course of antibiotics has finished, they can then go on to create an entire colony with the same genetic advantages. The antibiotic you took before will no longer be effective. The more antibiotics are used, the more this cycle repeats, and there are now several strains of bacteria that are able to resist the effects of some of our most powerful drugs. Even more worryingly, antibiotic resistance genes can be passed from one bacterium to the next and between species.

ANTIBIOTIC RESISTANCE

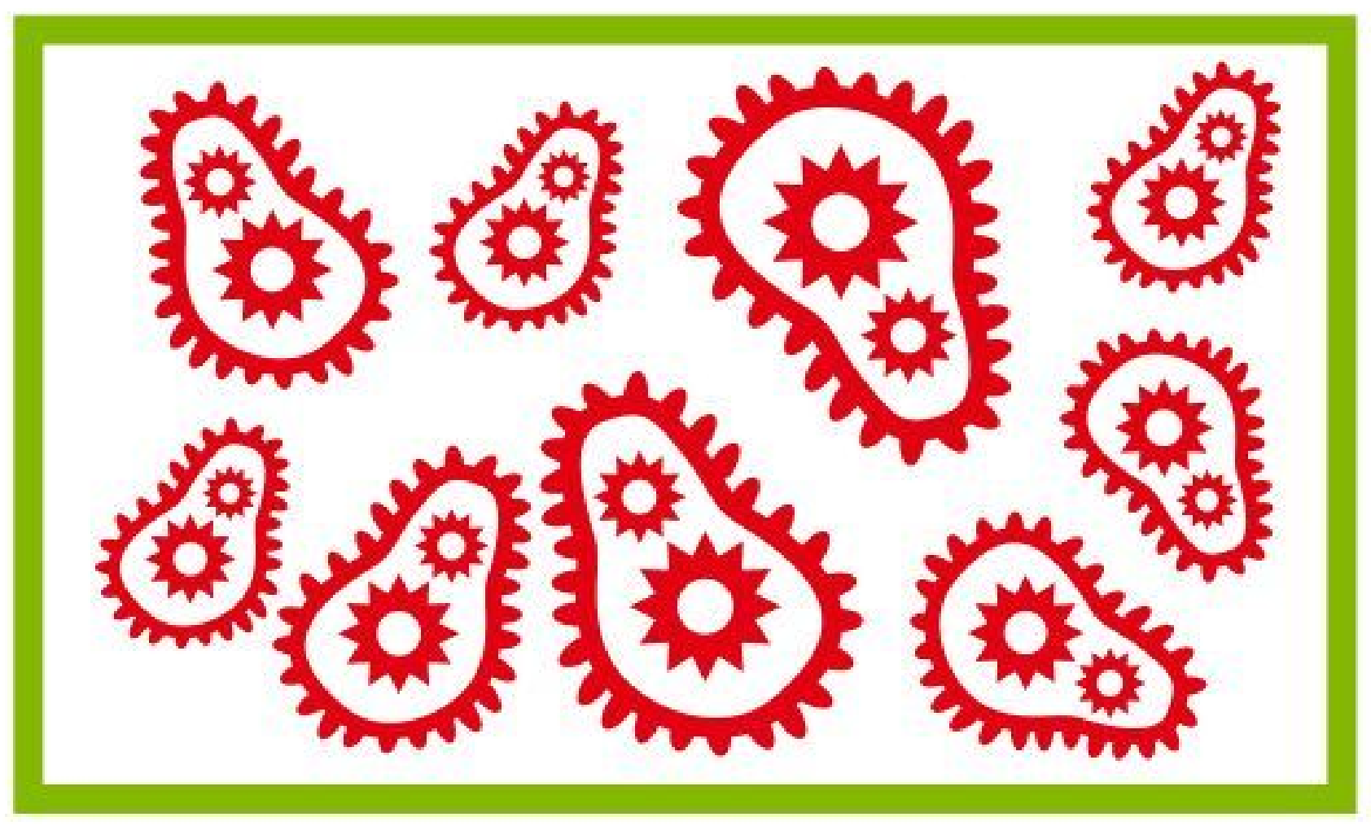
HOW DO BACTERIA MANAGE TO SURVIVE HIGH DOSES OF OUR MOST POWERFUL MEDICATIONS?



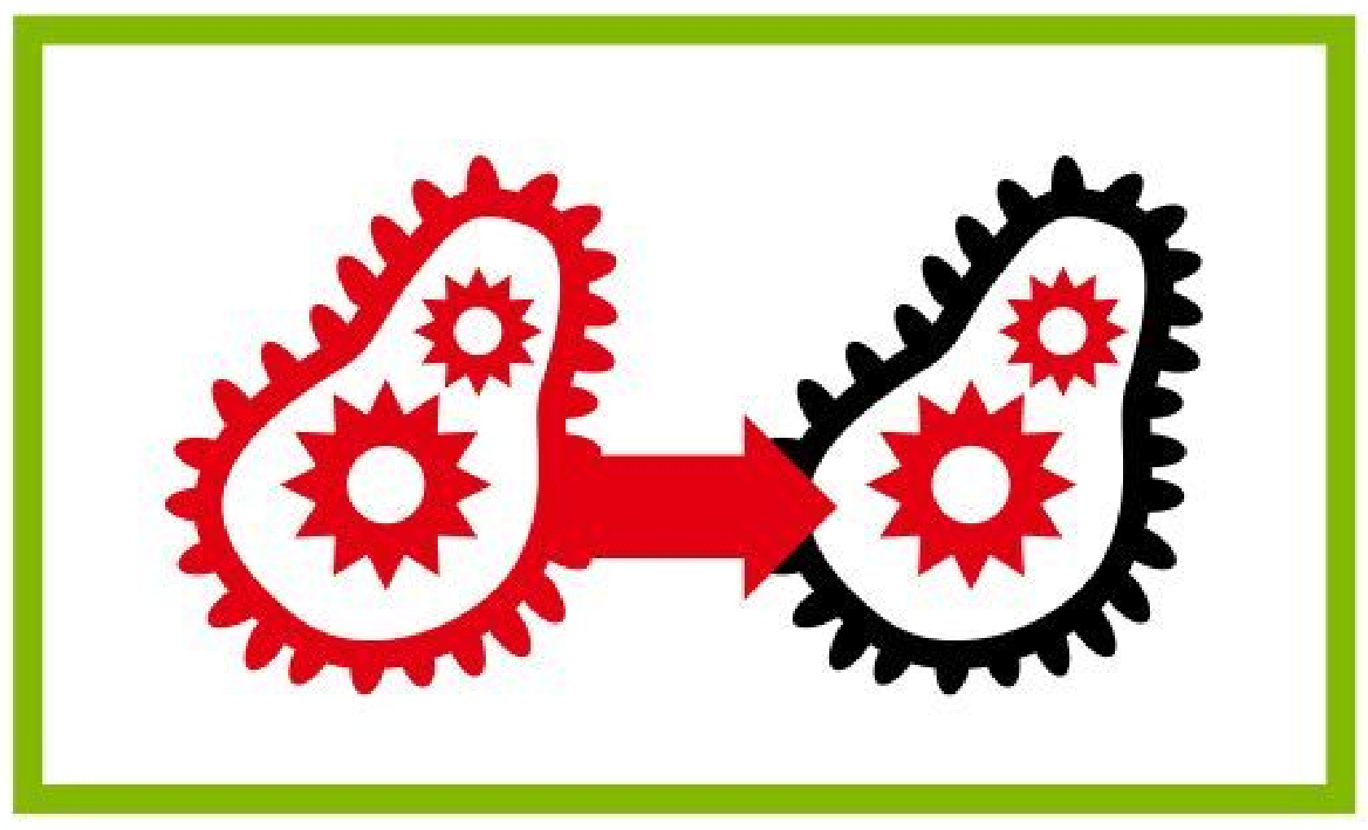
1 DIFFERENT GENES
Like humans, individual bacteria from the same species can have slightly different genetic profiles.



2 ANTIBIOTICS
Antibiotics kill bacteria or stop them dividing, and they can affect both 'good' and 'bad' bacteria.



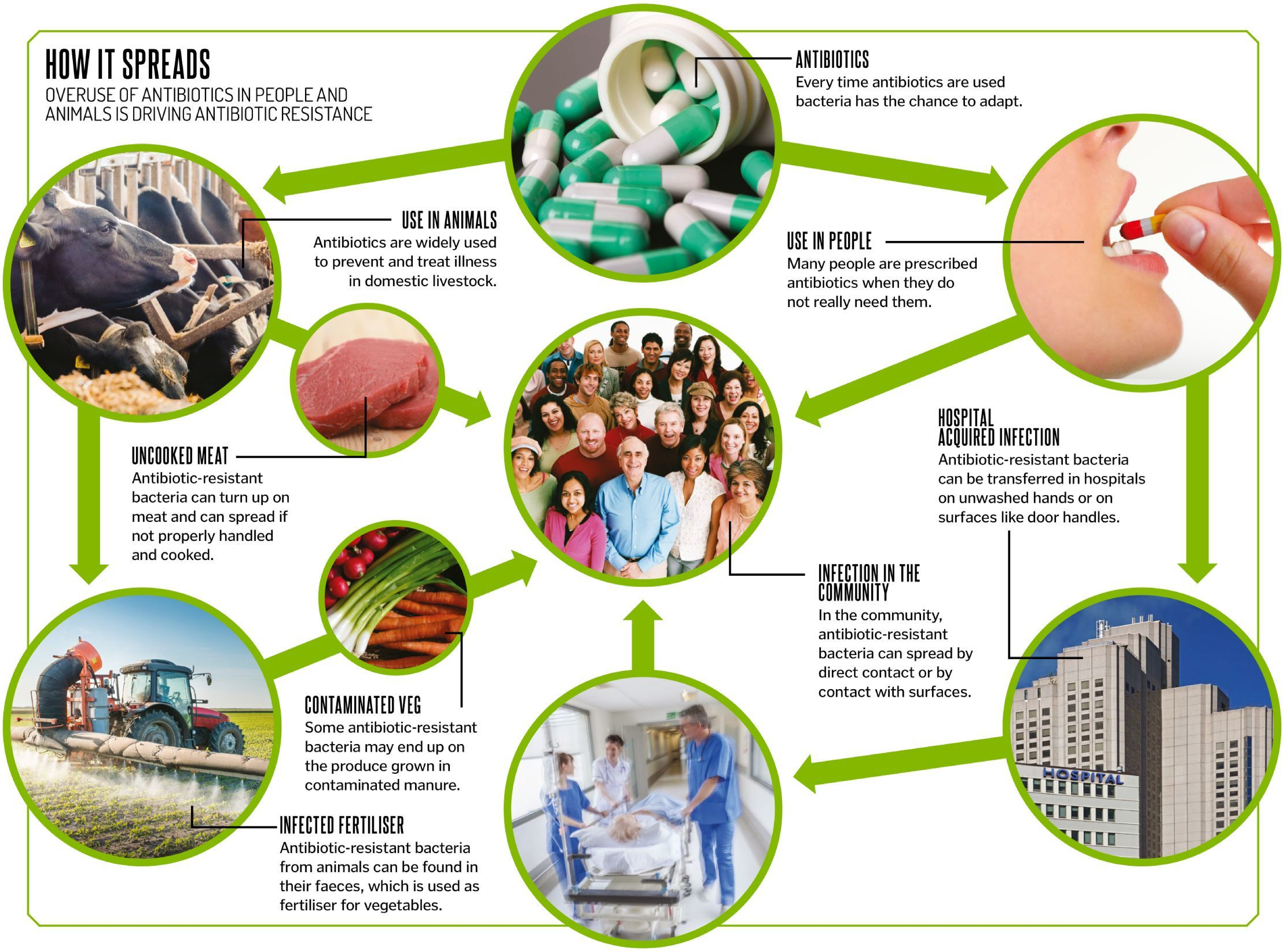
3 SOME SURVIVORS
Some bacteria have genetic traits that help them to survive antibiotic treatment, so they can continue dividing.



4 SHARING GENES
Resistant bacteria can sometimes pass their genes on to neighbouring bacteria, giving them resistance too.

HOW IT SPREADS

OVERUSE OF ANTIBIOTICS IN PEOPLE AND ANIMALS IS DRIVING ANTIBIOTIC RESISTANCE



ANTIBIOTICS
Every time antibiotics are used bacteria has the chance to adapt.

USE IN ANIMALS
Antibiotics are widely used to prevent and treat illness in domestic livestock.

USE IN PEOPLE
Many people are prescribed antibiotics when they do not really need them.

UNCOOKED MEAT
Antibiotic-resistant bacteria can turn up on meat and can spread if not properly handled and cooked.

HOSPITAL ACQUIRED INFECTION
Antibiotic-resistant bacteria can be transferred in hospitals on unwashed hands or on surfaces like door handles.

INFECTION IN THE COMMUNITY
In the community, antibiotic-resistant bacteria can spread by direct contact or by contact with surfaces.

CONTAMINATED VEG
Some antibiotic-resistant bacteria may end up on the produce grown in contaminated manure.

INFECTED FERTILISER
Antibiotic-resistant bacteria from animals can be found in their faeces, which is used as fertiliser for vegetables.

PERSONALISED MEDICINE

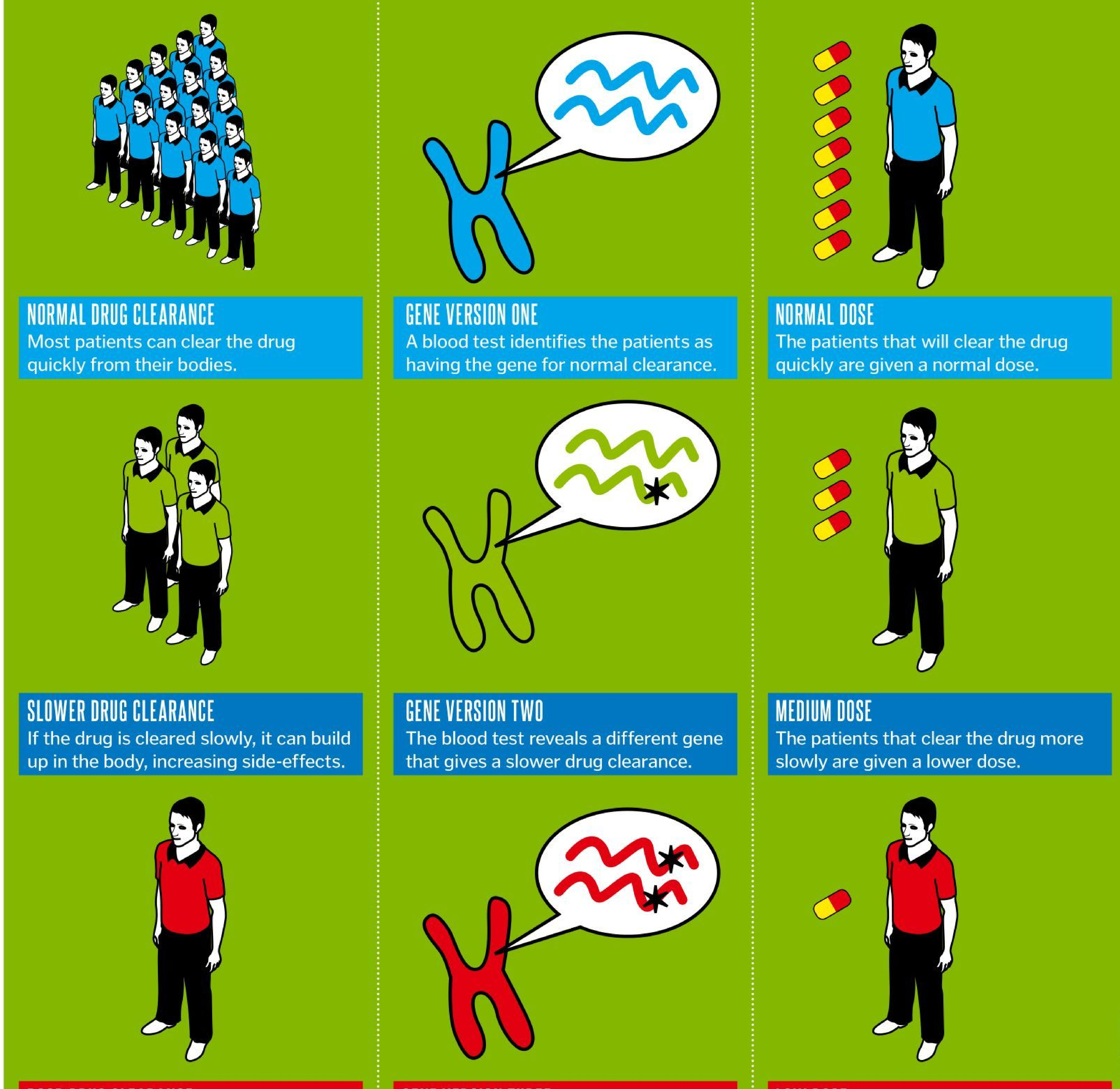
IN THE FUTURE, TREATMENTS WILL BE DESIGNED FOR YOUR UNIQUE GENETIC CHARACTERISTICS

The genetic differences that make us all unique also affect how we respond to medical treatment, and the genetic makeup of bacteria and viruses directly impacts their reaction to different drugs. Armed with an understanding of the genetics driving these different responses, we are moving towards an exciting time when treatments could be personally matched to each individual patient.

Steps are already being made with this kind of precision medicine in the treatment of cancer, where genetic differences in the tumour cells play a huge role in whether or not different treatments will work.

MATCHING MEDICINES TO GENETICS

PEOPLE HAVE DIFFERENT GENES, SO THEY RESPOND DIFFERENTLY TO THE SAME DRUGS

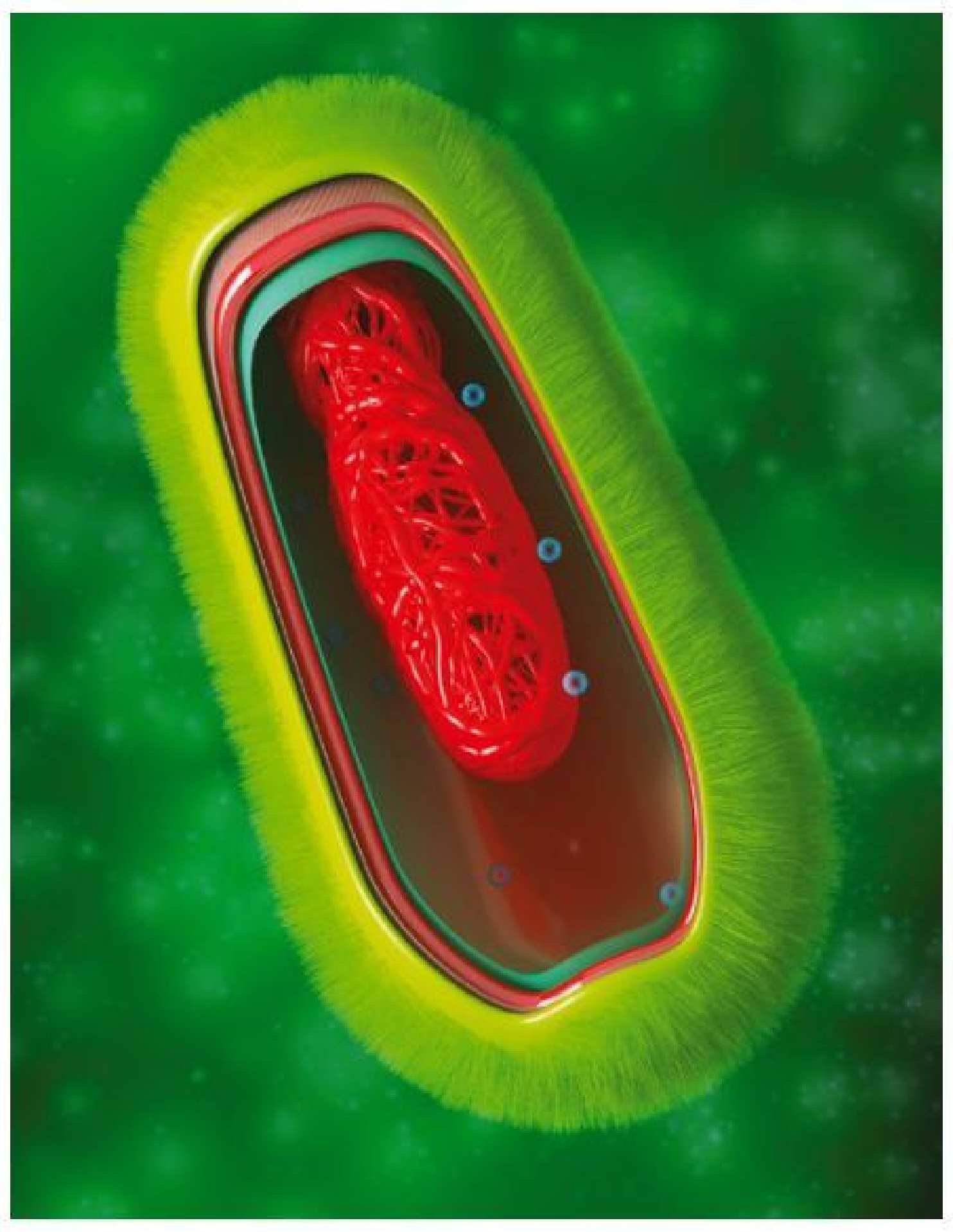


PATIENTS AWAITING TREATMENT These people all have the same cancer, but their genes are subtly different.	**DIFFERENT RESPONSES** Genetic differences affect how long it takes to clear the drug from the body.	**TAILORED DOSAGE** The patient can be given a dosage that matches their genetic makeup.
NORMAL DRUG CLEARANCE Most patients can clear the drug quickly from their bodies.	**GENE VERSION ONE** A blood test identifies the patients as having the gene for normal clearance.	**NORMAL DOSE** The patients that will clear the drug quickly are given a normal dose.
SLOWER DRUG CLEARANCE If the drug is cleared slowly, it can build up in the body, increasing side-effects.	**GENE VERSION TWO** The blood test reveals a different gene that gives a slower drug clearance.	**MEDIUM DOSE** The patients that clear the drug more slowly are given a lower dose.
POOR DRUG CLEARANCE A few patients clear the drug so slowly that normal doses become dangerous.	**GENE VERSION THREE** The gene identified in these patients means the drug will clear very slowly.	**LOW DOSE** The patients that struggle to clear the drug are given a small dose.

TEIXOBACTIN

THE FIRST NEW ANTIBIOTIC DISCOVERED IN 30 YEARS!

In 2015, scientists unveiled Teixobactin – a new antibiotic that has the potential to combat fatal infections such as pneumonia and tuberculosis. This latest discovery was found in the same source of many other antibiotics – soil – where it is produced naturally by other bacteria. It marks a huge step in the bid to control drug-resistant strains of superbugs.



○ Teixobactin stops bacteria from making the cell walls that they need in order to protect themselves

£10 MILLION PRIZE TO SOLVE ANTIBIOTIC RESISTANCE

The 2014 Longitude Prize encourages both amateur and professional scientists to develop a test that can be used to help doctors choose the right antibiotic quickly and cheaply. Ensuring that we only take antibiotics when we need them, and that we are only given ones that will work on our specific infection, is crucial if we want to slow antibiotic resistance.

○ The Longitude Committee will judge entries every four months until the end of 2019

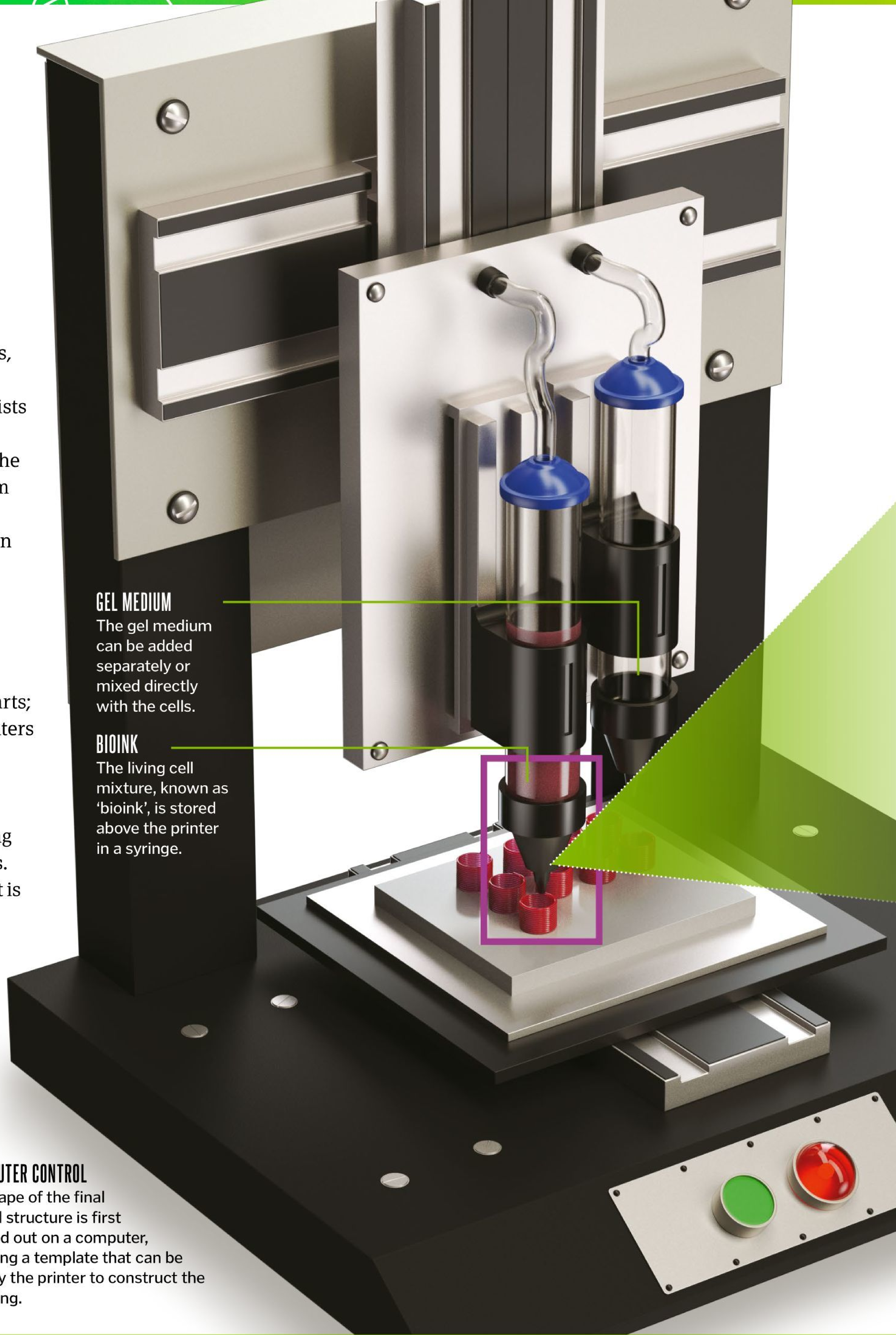
© Dreamstime; Thinkstock

PRINTING BODY PARTS

THE FUTURE HOLDS CUSTOM-PRINTED DRUGS AND PROSTHETICS, AND EVEN REPLACEMENT BODY PARTS

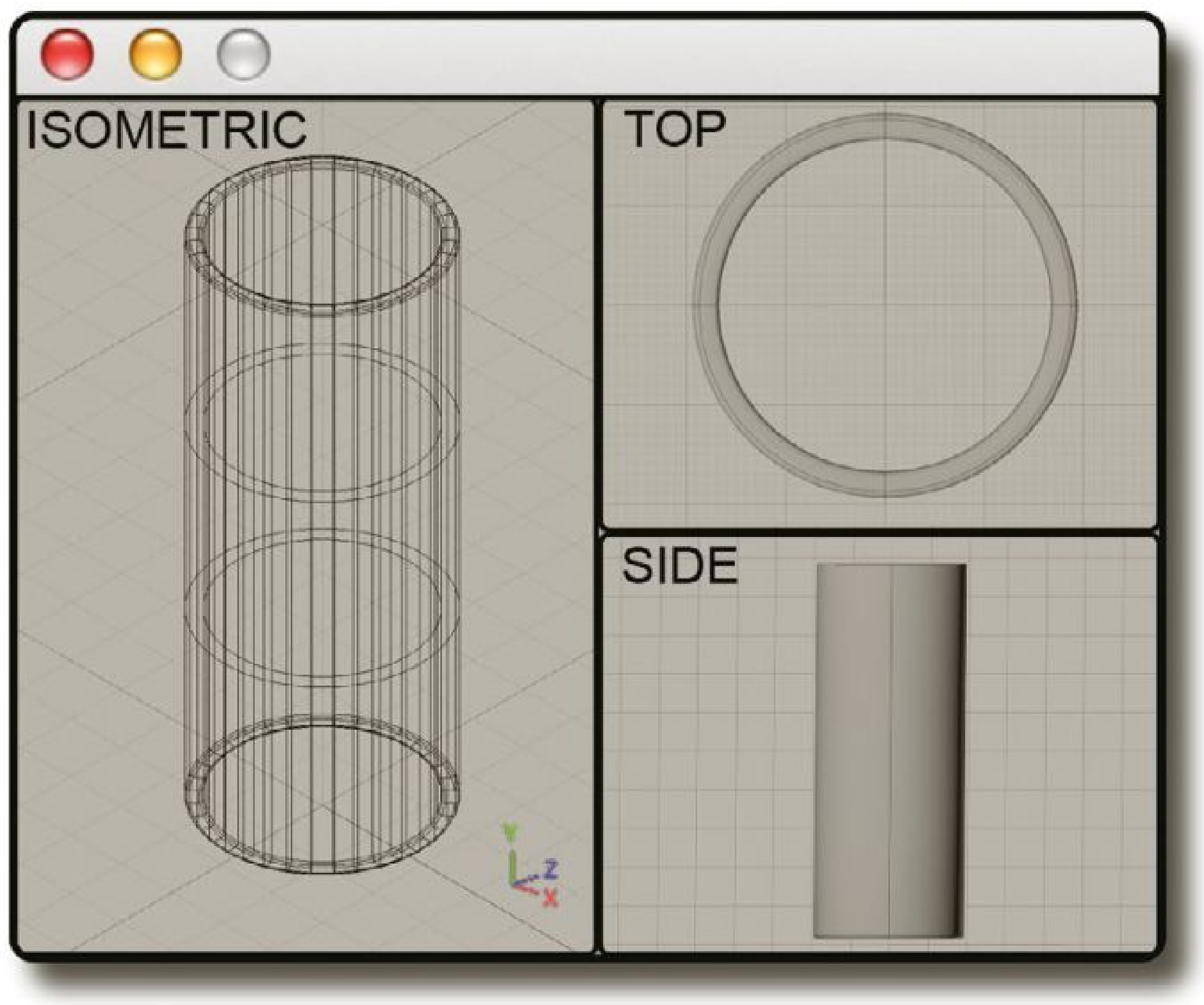
Plastic 3D printers are a natural fit for creating prosthetics, but some of the most exciting medical 3D printers use a different kind of 'ink'. Using precision techniques, scientists are working on combining different medicines into one compact pill. Different ingredients could be included in the printer to control when each drug is released, and custom pills could be printed for each patient. This goal is still decades away, but printers could be used to make vitamin supplements much sooner.

3D printers can also be used to create custom surgical implants, from plates, to replacement joints, to scaffolds used to encourage cells to grow into new tissues. These printed structures can either be long lasting or soluble. However, 3D printers don't just produce artificial body parts; they are also able to recreate the real thing. Some 3D printers are designed to print with living human cells, forming sheets of tissue that could be used as grafts to repair damage. Researchers at the Wake Forest Institute for Regenerative Medicine in North Carolina are also working on printing cells directly on to the body to repair wounds. Printing entire organs is the ultimate goal, but whether it is actually possible is a topic of debate among scientists.



GEL MEDIUM
The gel medium can be added separately or mixed directly with the cells.

BIOINK
The living cell mixture, known as 'bioink', is stored above the printer in a syringe.

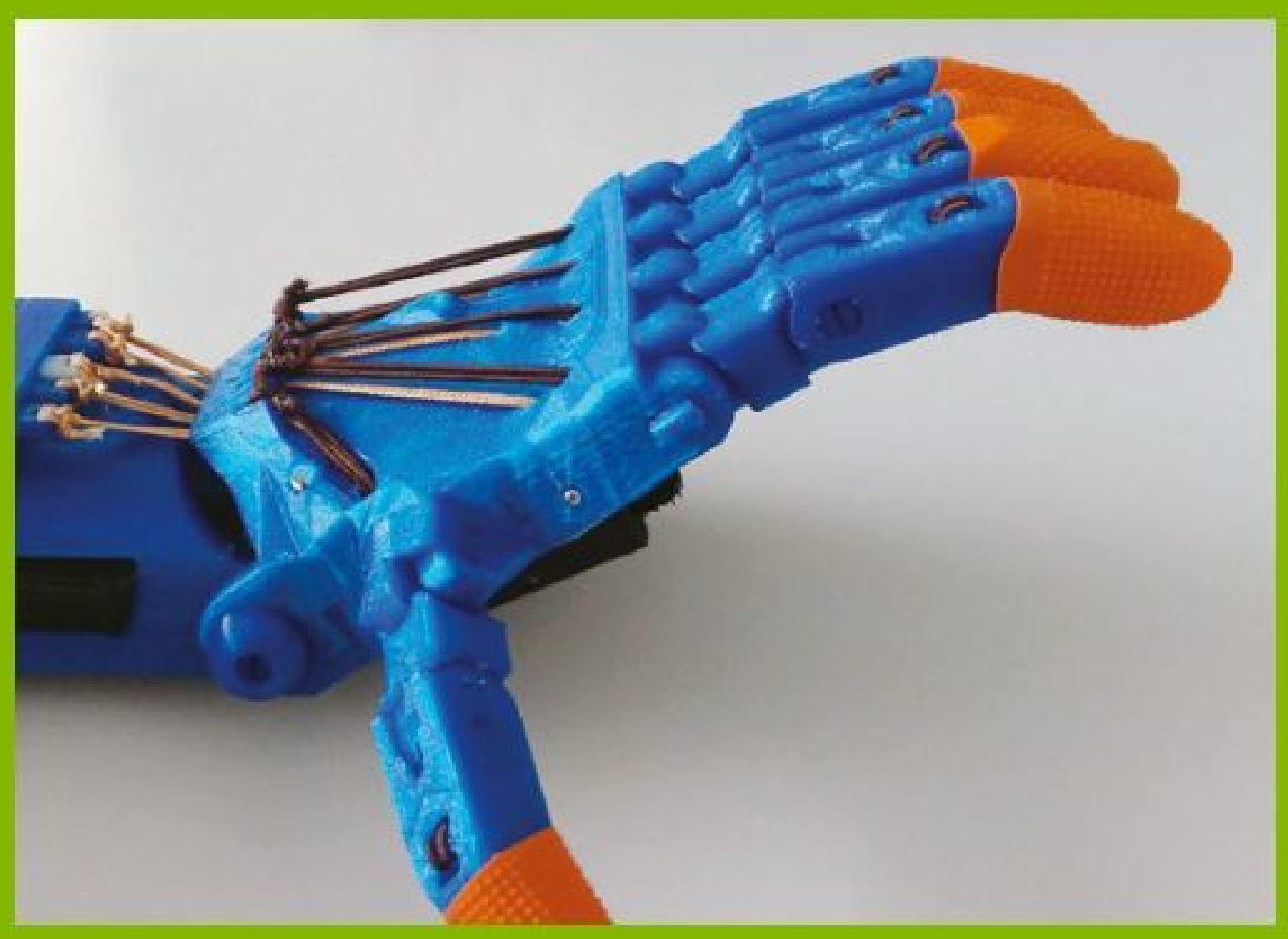


1 COMPUTER CONTROL
The shape of the final printed structure is first mapped out on a computer, providing a template that can be used by the printer to construct the real thing.

3D MEDICINE PRINTED MEDICAL SUPPLIES ARE ON THEIR WAY, AND SOME ARE ALREADY AVAILABLE

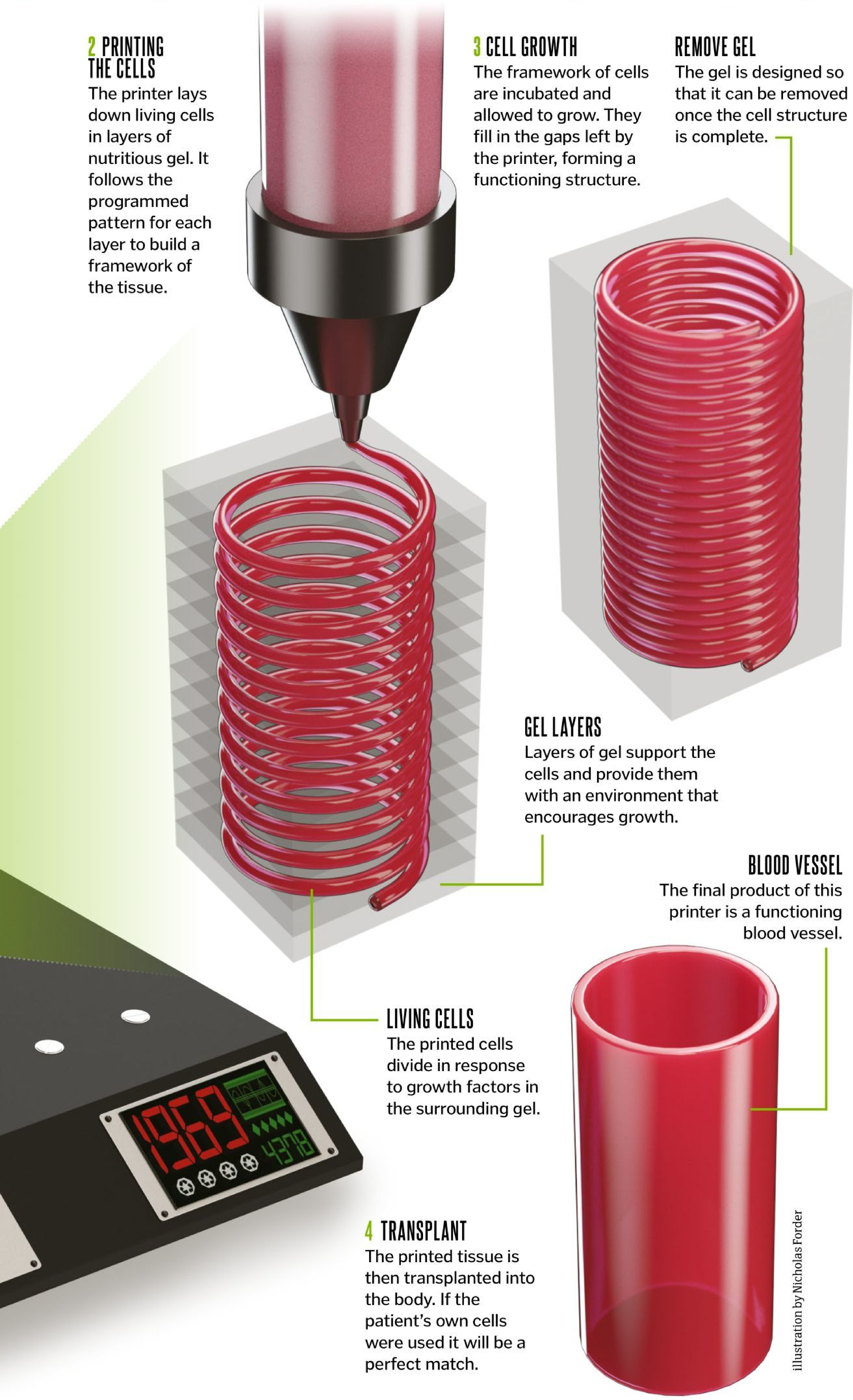
3D-PRINTED DRUGS

REPLACEMENT ORGANS



PROSTHETICS

DENTURES



2 PRINTING THE CELLS
The printer lays down living cells in layers of nutritious gel. It follows the programmed pattern for each layer to build a framework of the tissue.

3 CELL GROWTH
The framework of cells are incubated and allowed to grow. They fill in the gaps left by the printer, forming a functioning structure.

REMOVE GEL
The gel is designed so that it can be removed once the cell structure is complete.

GEL LAYERS
Layers of gel support the cells and provide them with an environment that encourages growth.

BLOOD VESSEL
The final product of this printer is a functioning blood vessel.

LIVING CELLS
The printed cells divide in response to growth factors in the surrounding gel.

4 TRANSPLANT
The printed tissue is then transplanted into the body. If the patient's own cells were used it will be a perfect match.

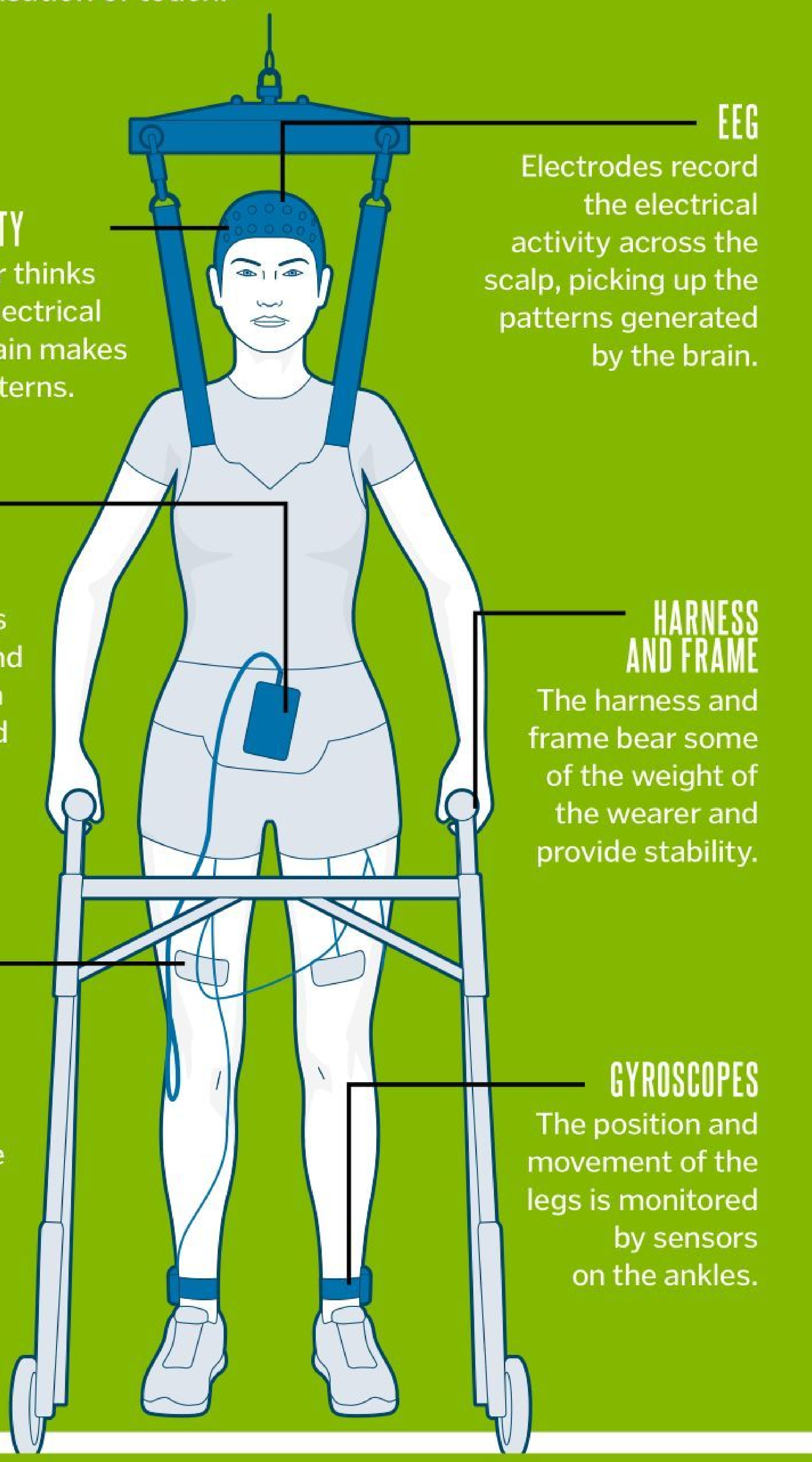
illustration by Nicholas Forder

HELPING PEOPLE TO WALK AGAIN

The future of medicine is not just about biological advancements – robotics, prosthetics and complex electronics are set to play an increasingly important role in health care. Existing medical prosthetics are able to respond to nerve impulses or muscle movements in the body of the wearer, and now research teams are plugging medical aids into the brain.

Brain-to-tech interfaces read the electrical patterns of the brain. These can be recorded across the scalp using an electroencephalogram (EEG), and the patterns can be decoded by a sophisticated computer algorithm. A team at the University of California, Irvine, have developed a system that monitors signals from the brain and transforms them into a series of electrical pulses. The pulses travel down wires attached to the muscles in the legs – effectively doing the job of the spinal cord.

The technology is still in development, but in early tests it enabled a man with a spinal cord injury to walk for the first time in seven years. Similar interfaces are also being trialled for use with prosthetics, and scientists are even working on sensors that can recreate the sensation of touch.



EEG
Electrodes record the electrical activity across the scalp, picking up the patterns generated by the brain.

ELECTRICAL ACTIVITY
When the wearer thinks about walking, electrical activity in the brain makes recognisable patterns.

PROCESSOR
A computer program interprets signals from the brain and creates a pattern of signals to send on to the legs.

HARNESS AND FRAME
The harness and frame bear some of the weight of the wearer and provide stability.

ELECTRODES
Electrodes attached to the knees deliver electrical impulses into the muscles that move the legs.

GYROSCOPES
The position and movement of the legs is monitored by sensors on the ankles.

SKIN GRAFTS

MEDICAL EQUIPMENT

SPLINTS, CASTS AND BRACES

BONE IMPLANTS

© Alamy; Rex Features

THE GENETIC REVOLUTION

FROM THE DISCOVERY OF DNA TO THE DAWN OF GENE EDITING IN LESS THAN 200 YEARS

In the 1800s, Swiss biologist Friedrich Miescher discovered something strange. When he broke open the nuclei of white blood cells he found a substance rich in phosphorous unlike anything he'd seen before. He named it nuclein. We now know it as DNA.

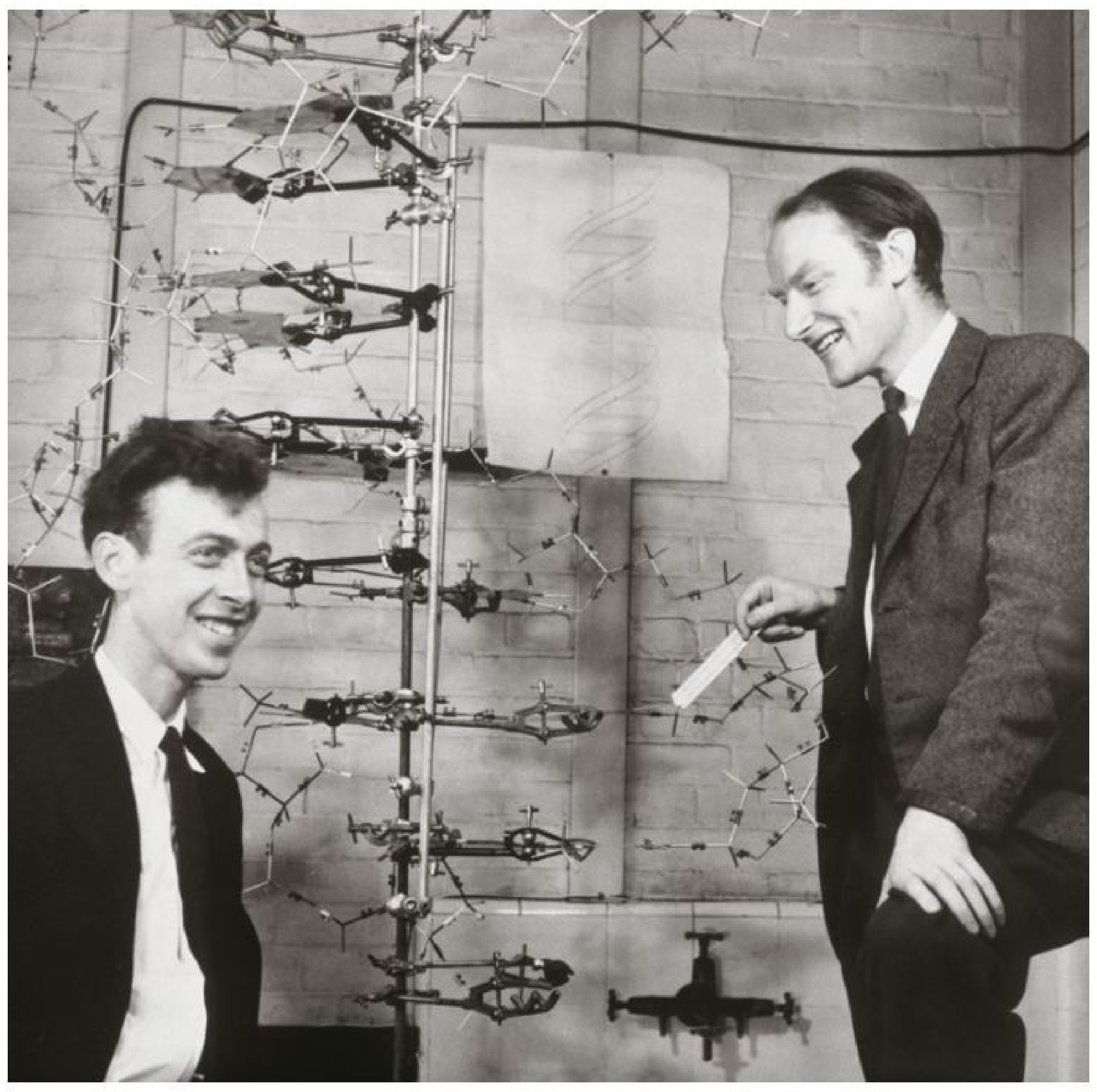
DNA stands for deoxyribonucleic acid. Thanks to the work of Russian-born American scientist Phoebus Levene we know that it has three parts. The phosphorous that Miescher noticed connects to a pentagon-shaped sugar called deoxyribose. This, in turn, links to a nitrogen-containing structure known as a 'base'. Four different bases make up the chemical letters of the genetic code, and the sugars and phosphates join them together into long strings.

The four DNA letters are adenine, cytosine, guanine and thymine. We know them most commonly by their first letter abbreviations: A, C, G and T. In a piece of DNA, the amount of A matches T and the amount of C matches G, but it wasn't until James Watson and Francis Crick that we found out why. This Nobel Prize-winning pair revealed the structure of the molecule.

Rosalind Franklin and Maurice Wilkins had taken a picture of DNA using X-rays. Using their images, along with cardboard cutouts of each of the DNA bases, Watson and Crick played with possible configurations. In 1953, they finally revealed that DNA is a double helix.

Two strands of code form a pair that wind around like a twisted ladder. The bases on one strand cling to the bases on another via interactions called hydrogen bonds, forming the ladder's rungs. The sugars and phosphates form the sides of the ladder, or the 'backbone'. Space between the rungs allows other molecules to read or copy the code.

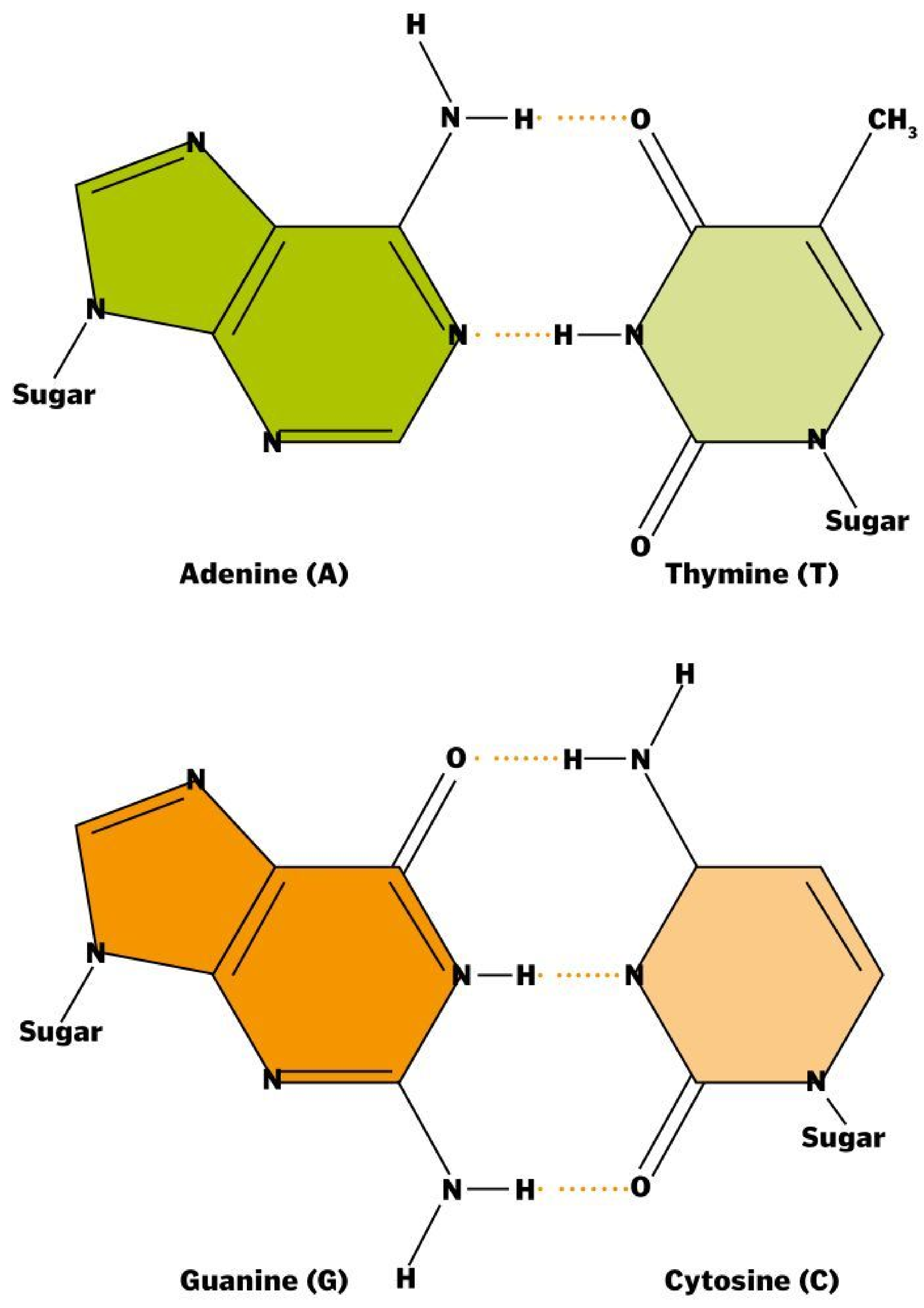
DNA has a right-handed curl, and the strands store opposite sequences running in opposite directions. The As on one strip cling to the Ts on the other, while the Cs partner up with Gs. One strand stores the code running top to bottom and the other stores the inverted code running bottom to top. Each strand has an up and a down, known to scientists as the 5' (pronounced five prime) and 3' (three prime) ends. These work a bit like having a capital letter at the start of a sentence and a full stop at the end, telling the cell in which direction it should read the code.



Watson and Crick standing next to their famous model of the DNA double helix

The structure of DNA has become iconic, but the distinctive twist is a frequent chemical quirk of biological molecules. The collagen strands in your skin twist like ropes, and so does the keratin in your hair. The building blocks of DNA are asymmetrical, and they stagger when stacked end-to-end. Once Watson and Crick revealed the structure, the next step was to crack the code. The scientific cryptographer responsible was Marshall Nirenberg.

Proteins make up most of the molecular machinery of the body, and cells build them from blocks called amino acids. There are 20 different blocks to choose from, so Nirenberg put each in a different tube. To understand what different DNA sequences meant he made synthetic strings of code. Then he watched to see which amino acids would be strung together with different sequences. His work revealed that DNA stores information as three-letter 'words'. There is a word for 'start', signalling the beginning of a gene, there are three words for 'stop', signalling the end, and between them there are 60 other three-letter 'codons' that correspond to amino acids.



Adenine always pairs with thymine and cytosine always pairs with guanine

With the cipher in hand, the next step was to decode the genome. To do this, Frederick Sanger invented DNA sequencing in 1977. His pioneering technique worked by breaking the code into overlapping chunks. He then copied each chunk in the presence of 'chain-terminating' nucleotides. These stop the copying process early, indicating which base just joined the end of the sequence. Bit by bit, the process reveals each letter of the code. Once he had the sequence for each chunk, Sanger could then stitch them back together like a jigsaw.

Armed with this new tool, scientists read the first full genome in 1995. It belonged to the bacterium *Haemophilus influenzae*. For the first time, scientists had the full instruction manual for making a living organism. In 2000, scientists

READING THE HUMAN GENOME

The Human Genome Project was one of the biggest scientific undertakings ever attempted. An international team of scientists worked together to read all 3.2 billion base pairs of human DNA. They mapped each human gene using a technique called bacterial artificial chromosome (BAC) sequencing.

First, they broke each chromosome into pieces around 200,000 base pairs long. Then they slotted them into 20,000 loops of DNA. Bacteria then copied the loops, building a vast DNA library. Scientists then cut the cloned DNA into 2,000 base pair fragments. A sequencer read the fragments, and they pieced the code back together by looking for areas that overlapped.

Before the project started people thought a genome as complicated as ours might contain more than 100,000 genes. However, when the results emerged it became clear that there were fewer than 25,000. Armed with this knowledge, scientists continue to explore our genetic code to find out where we came from, how we work and why our bodies go wrong.

The human genome project was an unprecedented feat of scientific cooperation

© SPL; Getty

finished the genetic code of the fruit fly. In 2002, they completed the mouse. And, a year later, the holy grail of sequencing emerged: the complete human genome.

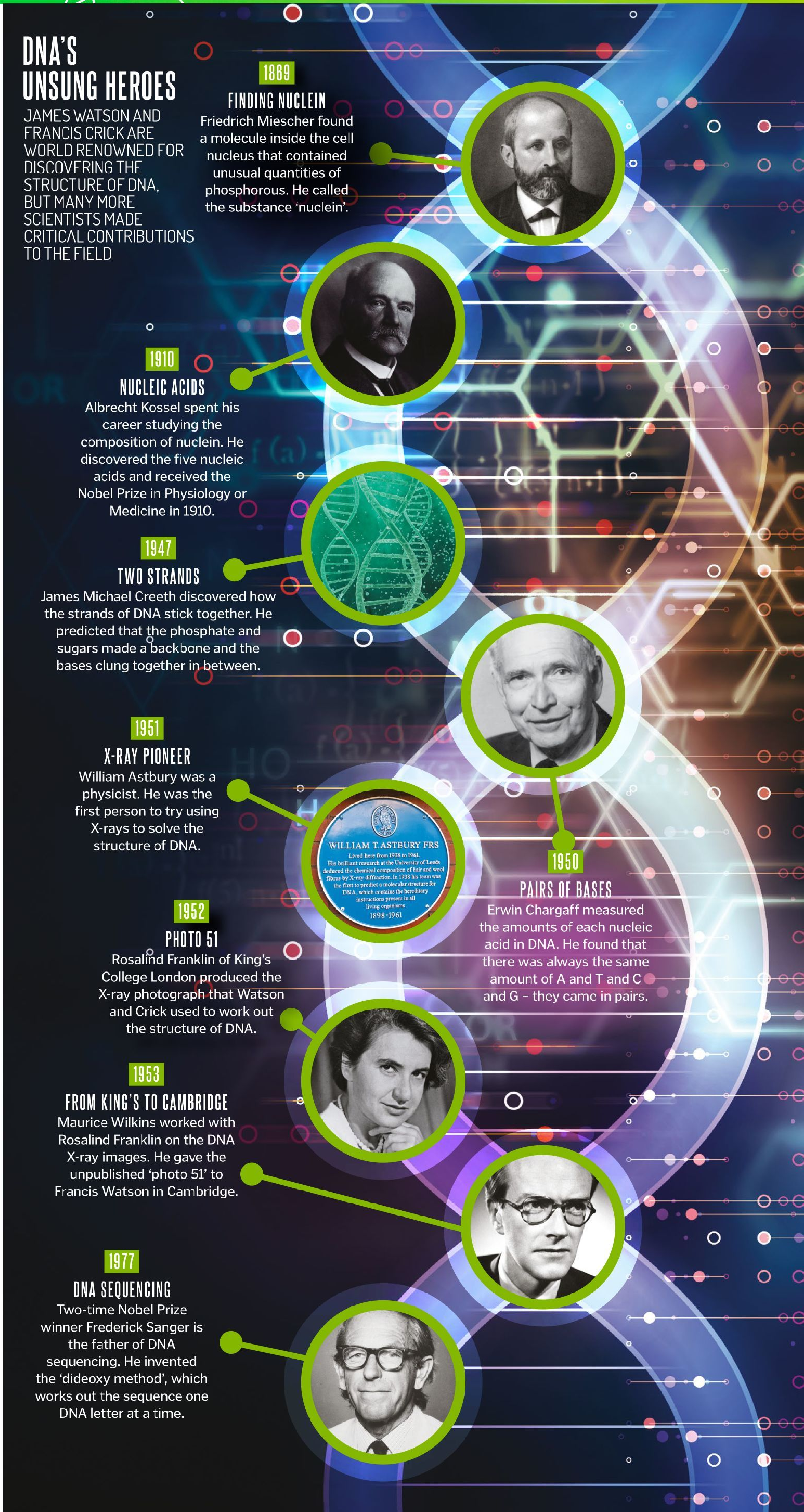
With access to these manuals, scientists could start to understand how things worked and why they go wrong. By the early 2000s they had amassed a powerful kit of molecular tools to help with their investigations. Even so, it would be an invention from two decades prior that would prove to be a pivotal piece in the mission to fully decode human DNA.

In 1983 an American biochemist by the name of Kary Mullis invented a technique called polymerase chain reaction (PCR), an accomplishment for which he received the Nobel Prize in Chemistry in 1993. PCR is a DNA photocopier that can make millions of identical sequences from one DNA strand. First, the temperature rises, splitting the double helix apart. Then an enzyme called a polymerase runs along and copies the DNA. Finally, the temperature drops and the strands find a matching pair to form a double helix again. Scientists can choose where to start and stop the copying process by using short stretches of DNA called primers. With this tool at their disposal it became even easier to study individual genes.

Scientists also had access to molecular scissors called restriction enzymes. These cut DNA in specific places, often leaving a little overhang. The 'sticky ends' let scientists glue different

> *"With access to these manuals, scientists could start to understand how things worked"*

○ Berkeley scientist Jennifer Doudna invented the CRISPR gene-editing technique


WILLIAM T. ASTBURY FRS
Lived here from 1928 to 1961.
His brilliant research at the University of Leeds deduced the chemical composition of hair and wool fibres by X-ray diffraction. In 1938 his team was the first to predict a molecular structure for DNA, which contains the hereditary instructions present in all living organisms.
1898-1961

DNA'S UNSUNG HEROES

JAMES WATSON AND FRANCIS CRICK ARE WORLD RENOWNED FOR DISCOVERING THE STRUCTURE OF DNA, BUT MANY MORE SCIENTISTS MADE CRITICAL CONTRIBUTIONS TO THE FIELD

1869

FINDING NUCLEIN

Friedrich Miescher found a molecule inside the cell nucleus that contained unusual quantities of phosphorous. He called the substance 'nuclein'.

1910

NUCLEIC ACIDS

Albrecht Kossel spent his career studying the composition of nuclein. He discovered the five nucleic acids and received the Nobel Prize in Physiology or Medicine in 1910.

1947

TWO STRANDS

James Michael Creeth discovered how the strands of DNA stick together. He predicted that the phosphate and sugars made a backbone and the bases clung together in between.

1951

X-RAY PIONEER

William Astbury was a physicist. He was the first person to try using X-rays to solve the structure of DNA.

1950

PAIRS OF BASES

Erwin Chargaff measured the amounts of each nucleic acid in DNA. He found that there was always the same amount of A and T and C and G – they came in pairs.

1952

PHOTO 51

Rosalind Franklin of King's College London produced the X-ray photograph that Watson and Crick used to work out the structure of DNA.

1953

FROM KING'S TO CAMBRIDGE

Maurice Wilkins worked with Rosalind Franklin on the DNA X-ray images. He gave the unpublished 'photo 51' to Francis Watson in Cambridge.

1977

DNA SEQUENCING

Two-time Nobel Prize winner Frederick Sanger is the father of DNA sequencing. He invented the 'dideoxy method', which works out the sequence one DNA letter at a time.

A REVOLUTION IN GENE EDITING

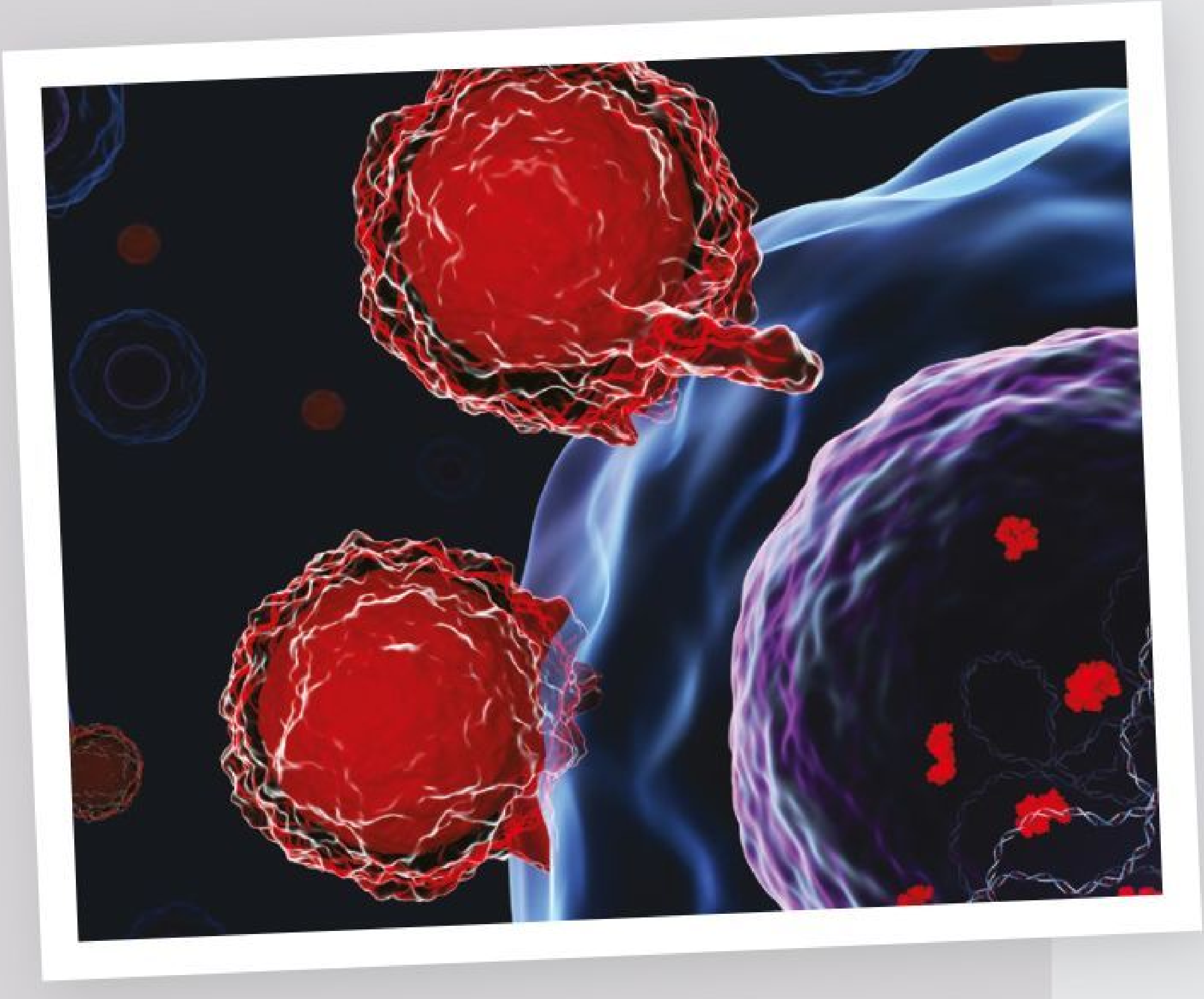
PRECISION GENE EDITING WITH CRISPR-CAS9 COULD CHANGE THE WAY WE INTERACT WITH OUR GENOME

CRISPR stands for 'Clustered Regularly Interspaced Short Palindromic Repeat'. The acronym describes sections of DNA that read the same forwards and backwards (palindromes). They occur in groups in some types of bacteria and archaea, forming part of their defence against viruses.

When a virus invades, the bacterium cuts out a piece of its genetic code and slots it between two CRISPR sequences. It then makes copies of the CRISPR DNA and the viral DNA sandwiched between. The copies, made from RNA, are like DNA but exist as single strands instead of double helixes. This means that the unpaired bases are free to stick to any matching code that they find inside the cell. If the same virus attacks again, the RNA sticks to its genetic code.
This is where the second part of the system comes in.

CRISPR works together with molecules called Cas (which stands for CRISPR-associated). They are gene-snipping molecular scissors, and the RNA carries Cas to the matching viral genetic code, enabling Cas to cut it up. Scientists can hijack the system for genetic engineering by replacing the RNA with a sequence of their own. By designing the sequence to match part of a gene, they can guide the molecular scissors to make specific cuts in the genome.

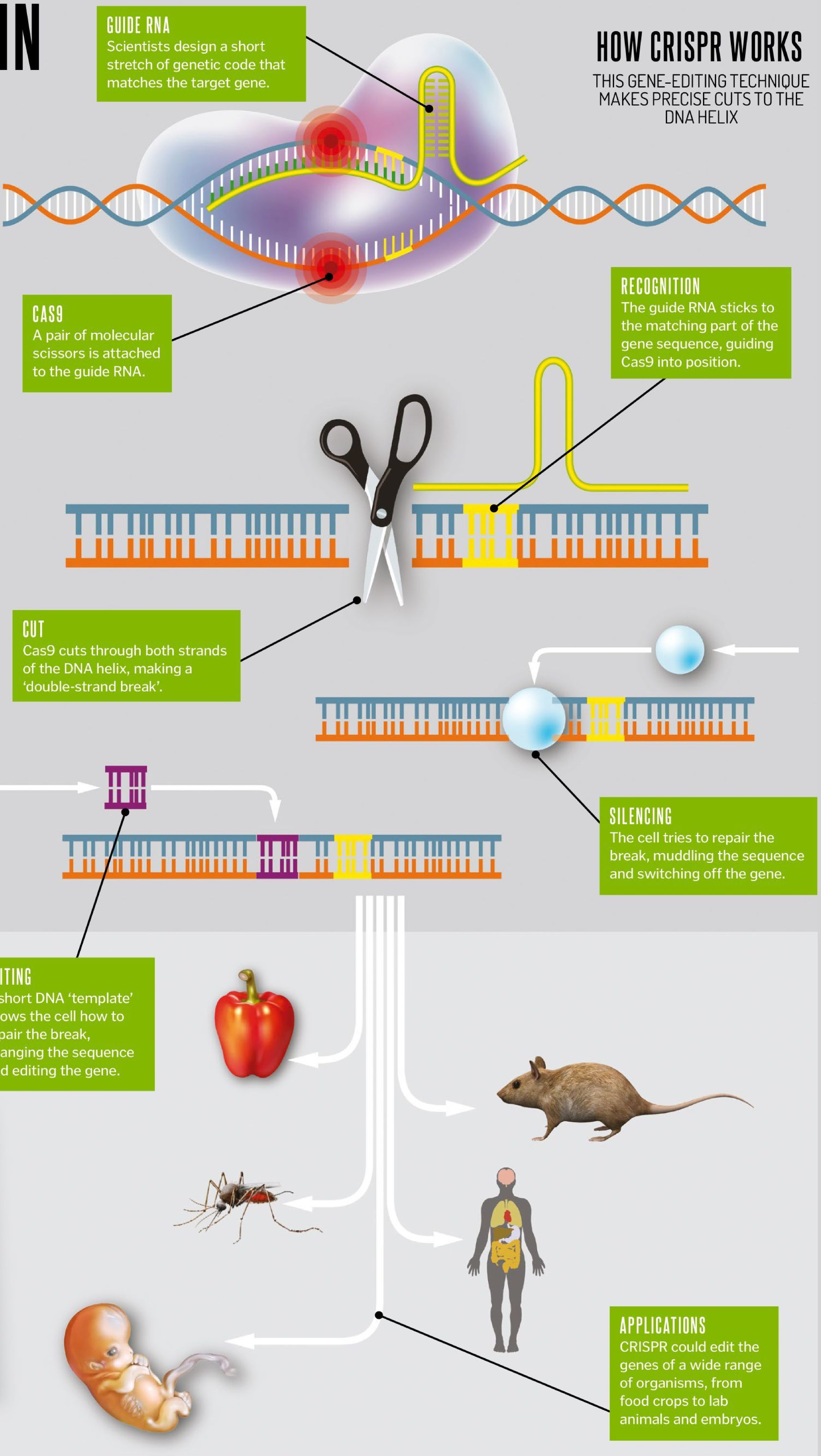
When the cell tries to repair the cut it often makes mistakes. This disrupts the gene, switching it off – a process known as silencing. If the scientists provide a DNA template, the cell can use it as a guide to repair the break, making edits to the gene.



○ CRISPR could be used to help the immune system fight cancer

HOW CRISPR WORKS

THIS GENE-EDITING TECHNIQUE MAKES PRECISE CUTS TO THE DNA HELIX



GUIDE RNA
Scientists design a short stretch of genetic code that matches the target gene.

CAS9
A pair of molecular scissors is attached to the guide RNA.

RECOGNITION
The guide RNA sticks to the matching part of the gene sequence, guiding Cas9 into position.

CUT
Cas9 cuts through both strands of the DNA helix, making a 'double-strand break'.

SILENCING
The cell tries to repair the break, muddling the sequence and switching off the gene.

EDITING
A short DNA 'template' shows the cell how to repair the break, changing the sequence and editing the gene.

APPLICATIONS
CRISPR could edit the genes of a wide range of organisms, from food crops to lab animals and embryos.

© Getty; University of Nottingham; Wiki/ Wellcome Images/ Kamil Kroplewski; SPL

UNRAVELLING DNA REPAIR

In 2015, Tomas Lindahl, Paul Modrich and Aziz Sancar received the Nobel Prize in Chemistry for their work on DNA repair.

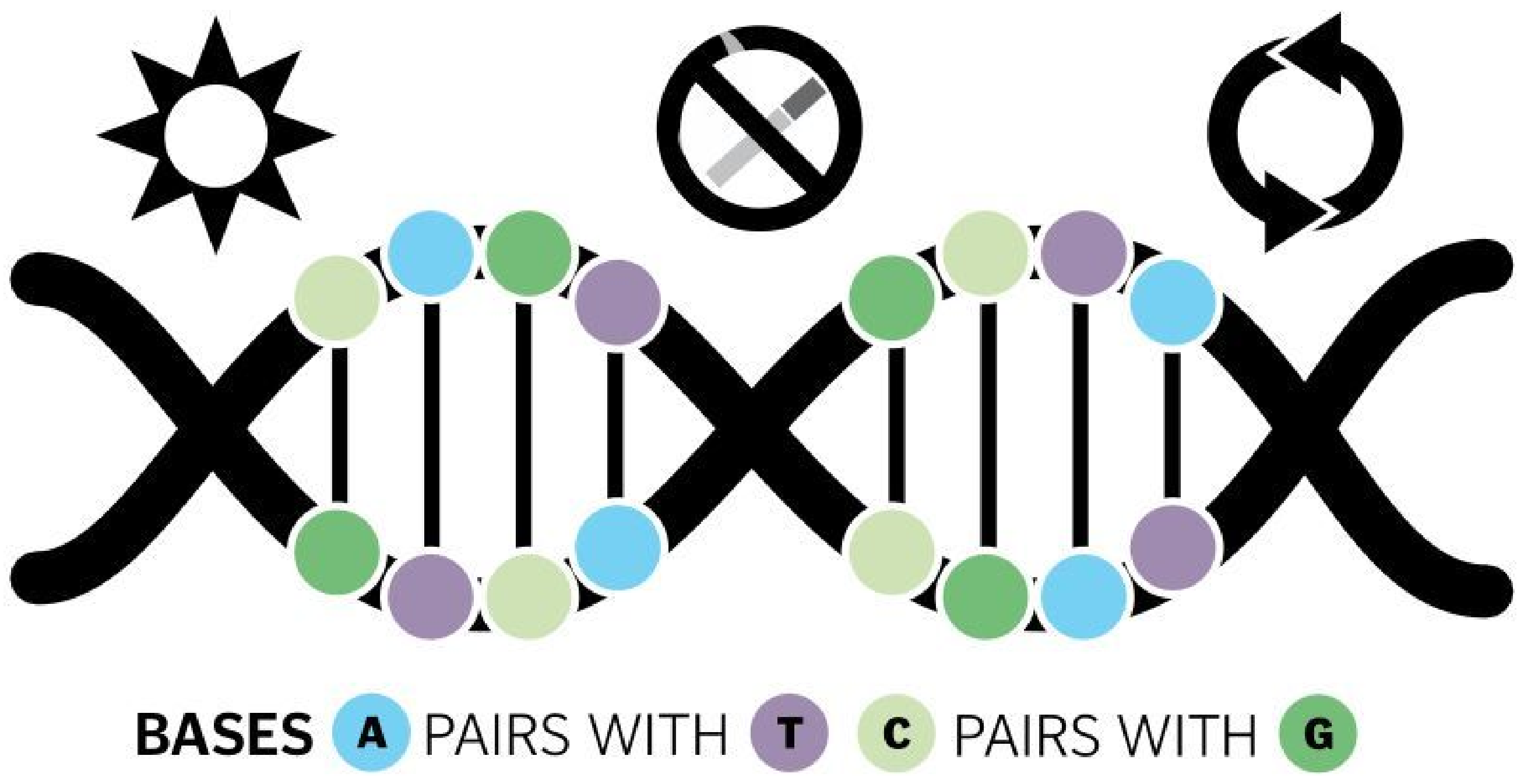
Throughout our lives, our DNA is continuously under assault from the environment. Ultraviolet light sticks DNA bases together and cigarette smoke can cause mutations. Every time a cell divides, it makes small copying errors. The separate work of these scientists delved into the microscopic machinery that finds this damage and fixes it.

Lindahl discovered 'base excision repair', a process that cuts small errors from the genome and remakes them. Sancar found a similar system called 'nucleotide excision repair', which removes and fixes errors that make the DNA bulge. Modrich identified DNA 'mismatch repair', which fixes areas where bases on opposite strands don't match up. Understanding how these tools work is the vital first step in finding out how best to use them going forward.

○ The fluorescent bands on this gel are fragments of DNA

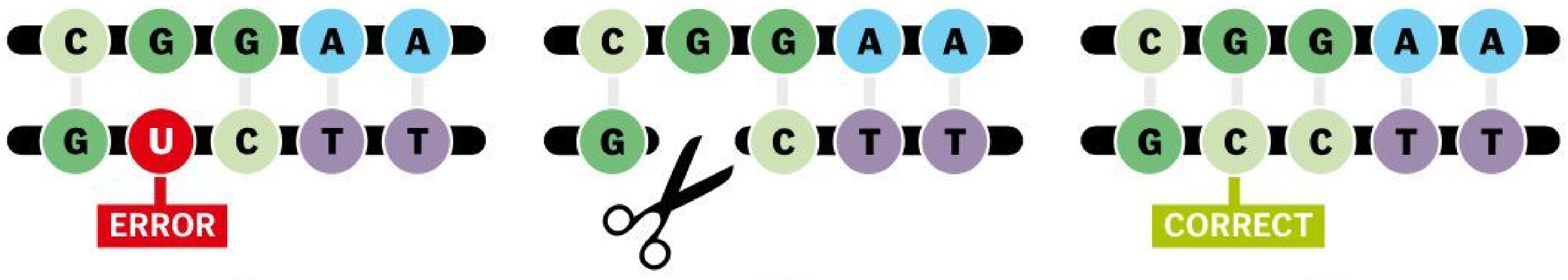
DNA DAMAGE

DNA accumulates errors over time. Some occur when cells make copying mistakes. Others are the result of an environmental attack from carcinogens like UV light, radiation or cigarette smoke.


BASES A PAIRS WITH T C PAIRS WITH G

Base excision repair

Chemical changes can alter the structure of bases over time. Lindahl discovered base excision repair, which cuts out the damaged areas and replaces them.


C G G A A
G U C T T
ERROR
C G G A A
G C T T
C G G A A
G C C T T
CORRECT

1

C loses an amino group to form U. U can't pair with G.

2

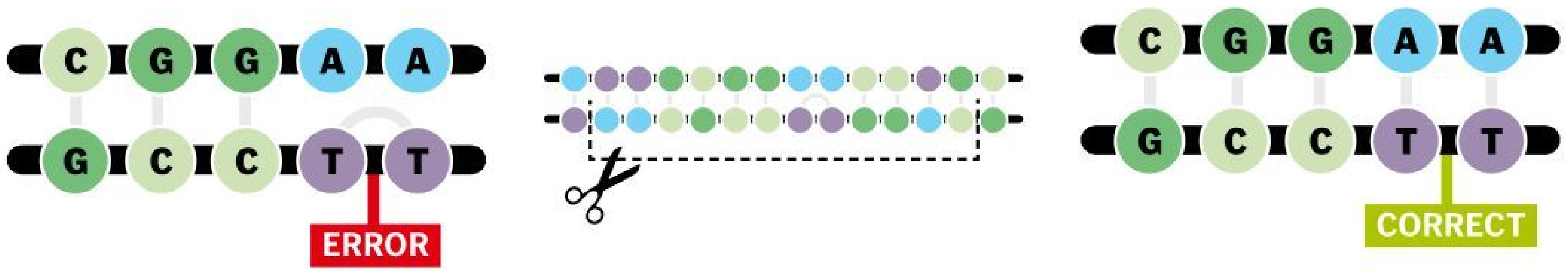
Enzymes remove U and its section of the DNA strand.

3

The correct base is inserted and the strand sealed.

Nucleotide excision repair

Environmental agents like UV light can stick adjacent bases together, forming bulges. Sancar discovered nucleotide excision repair, which recognises and repairs these errors.


C G G A A
G C C T T
ERROR
C G G A A
G C C T T
CORRECT

1

UV radiation can cause two Ts to bind to each other.

2

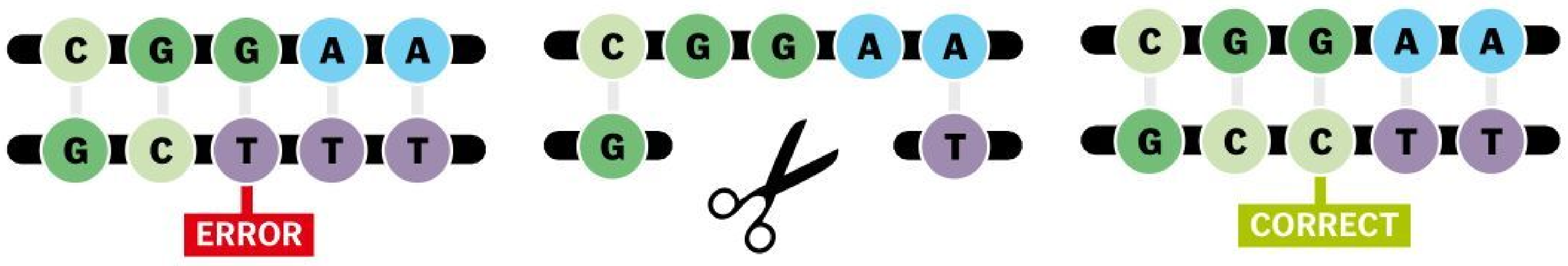
An enzyme cuts a 12-nucleotide strand, removing damage.

3

The resulting gap in the DNA is filled and then sealed.

Mismatch repair

Cells make errors as they copy their genetic code. Modrich found the system that corrects these errors by cutting them out and replacing them with the correct bases.


C G G A A
G C T T T
ERROR
C G G A A
G T
C G G A A
G C C T T
CORRECT

1

Sometimes the nucleotides in copied DNA don't match.

2

Enzymes remove a section containing the faulty nucleotide.

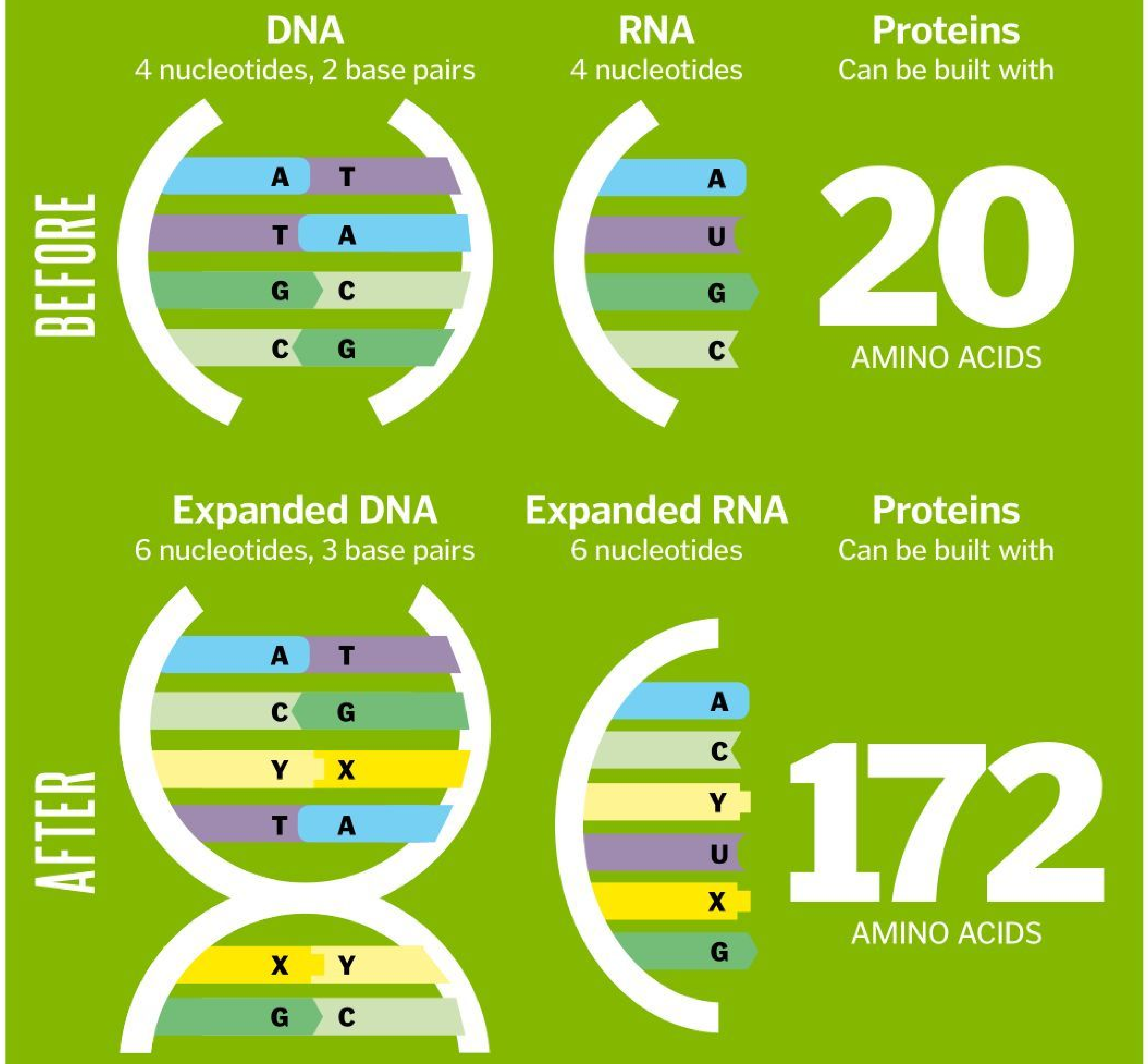
3

The resulting gap in the DNA is filled and then sealed.

EXPANDING THE GENETIC CODE

In 2017, a team of scientists from California increased the size of the DNA alphabet. In 2014, they had succeeded in getting E coli bacteria to put different chemical bases into their DNA. However, at the time the extra letters were silent – they stayed in the genetic code, but they didn't spell anything useful.

Now they've upgraded the cells so that they can use the code to make 'designer proteins'. In nature, cells work with a toolbox of 20 amino acids, but more exist artificially. Extra letters open up the possibility to write new genetic words that code for these amino acids. In the latest study, bacteria put unnatural bases into their DNA. They then used the new code to add unusual amino acids to their proteins.


DNA
4 nucleotides, 2 base pairs
RNA
4 nucleotides
Proteins
Can be built with
BEFORE
A T
T A
G C
C G
A
U
G
C
20
AMINO ACIDS
Expanded DNA
6 nucleotides, 3 base pairs
Expanded RNA
6 nucleotides
Proteins
Can be built with
AFTER
A T
C G
Y X
T A
X Y
G C
A
C
Y
U
X
G
172
AMINO ACIDS

○ Scientists are trying to make designer proteins using new genetic bases and synthetic amino acids chunks of DNA together, opening the door to genetic engineering.

Using PCR, scientists can make copies of a gene they're interested in. Then they cut open a circle of bacterial DNA, called a plasmid. They stitch the gene into place and put the plasmid back into bacteria so that the microbes can read the code. The bacteria use the gene as if it were their own, decoding the three-letter words and stringing amino acids end-to-end to make protein. The pharmaceutical industry uses this technique to make human insulin to treat diabetes, and it's widely employed in labs to manufacture protein for research. But bacteria aren't the only organisms that will accept foreign DNA. Biologists can also put genes into animal or human cells in a process called transformation.

Human cells don't use plasmids in the same way as bacteria, but there's a small chance that genetic code carried into the cell will fuse with the genome. In the early days of genetic engineering, scientists boosted the chances by making breaks in the genetic code. As the cell repaired the strand the new DNA became a template. It worked, but it was hard to direct the genetic edits to the right place.

Then, in the 1990s, scientists discovered 'programmable nucleases'. These molecules have two parts: one sticks to specific sequences of DNA, and the other cuts through the strands. Scientists can design stretches of DNA to match specific parts of the genome, allowing them to direct the DNA scissors to precise parts of a gene.

The first programmable nucleases were 'zinc finger nucleases'. Zinc fingers are twists of protein that recognise three base pairs of DNA, and DNA scissors can be used to shorten the sequences of bases, but they aren't always accurate. They have so called 'off-target effects', often taking the scissors to more than one section of DNA by mistake.

○ This device is a prototype of one of the first DNA-photocopying PCR machines of the 1980s

The next step up was the transcription activator-like effector nucleases, or TALENs. These contain TAL effectors: proteins made by bacteria that recognise DNA. The repeats recognise one base at a time, making them more precise than zinc fingers. The latest and most exciting programmable nuclease is CRISPR, which promises precision never seen before.

With these tools at our disposal, genetic engineering is now commonplace in biomedical research. Scientists use it to switch genes on and off to study their effects. They make edits to the genomes of cells and animals, and they manipulate genetic information to look for the changes that might cause disease. They put human genes into animals to see what they do; they hijack bacteria to make vast quantities of protein; and they transfer genes from one animal to another. Genes from fluorescent jellyfish proteins are used to make other animals glow, for example. Genetic engineering is also finding its way into everyday life. It gave us insulin to treat diabetes, vitamin A-rich golden rice and soybeans resistant to weed-killers. It's now starting to make its way into medicine too.

In the early 2000s, 13 children underwent gene therapy to repair a faulty gene that was stopping their immune systems from working. The technique cured nine of the children, but it wasn't perfect. Two went on to develop leukaemia. The repaired gene had inserted into the wrong part of the genome, disrupting a gene involved in preventing cancer.

> "Genetic engineering is now commonplace in biomedical research"

For genetic engineering to become a powerful clinical tool we need more control. CRISPR promises better precision, but research is ongoing. Being able to read the genome could point to the errors that cause human disease. Being able to edit it could help us to fix them.

In the future, genetic engineering could bring us new fuels, chemicals and drugs. It could help us to increase the size of plants and animals and boost their resistance to disease. It could help endangered species to cope with changing environments or resurrect extinct animals. It might even change what it means to be human.

IS IT RIGHT TO PLAY WITH OUR GENES?

Genetic engineering is amazing, but many people worry about the consequences. At the moment most gene editing takes place in research labs, but in the future it could find more and more uses in the real world. One goal is to use technologies like CRISPR to repair faulty genes in the cells of sick children and adults. This might treat their illness, but the genetic changes wouldn't pass on to their offspring.

Another option is to make changes to sperm and egg cells. The genetic repairs would then pass to the next generation and every generation afterwards. But making permanent changes to the human gene pool is risky. Some people worry that we don't yet understand the human genome, or the tools, well enough to ensure that the edits will be safe. Others worry that it's the start of a slippery slope to designer babies. At present many countries ban this type of 'germline' gene editing.

○ Should we use gene-editing technologies to make permanent changes to human DNA?

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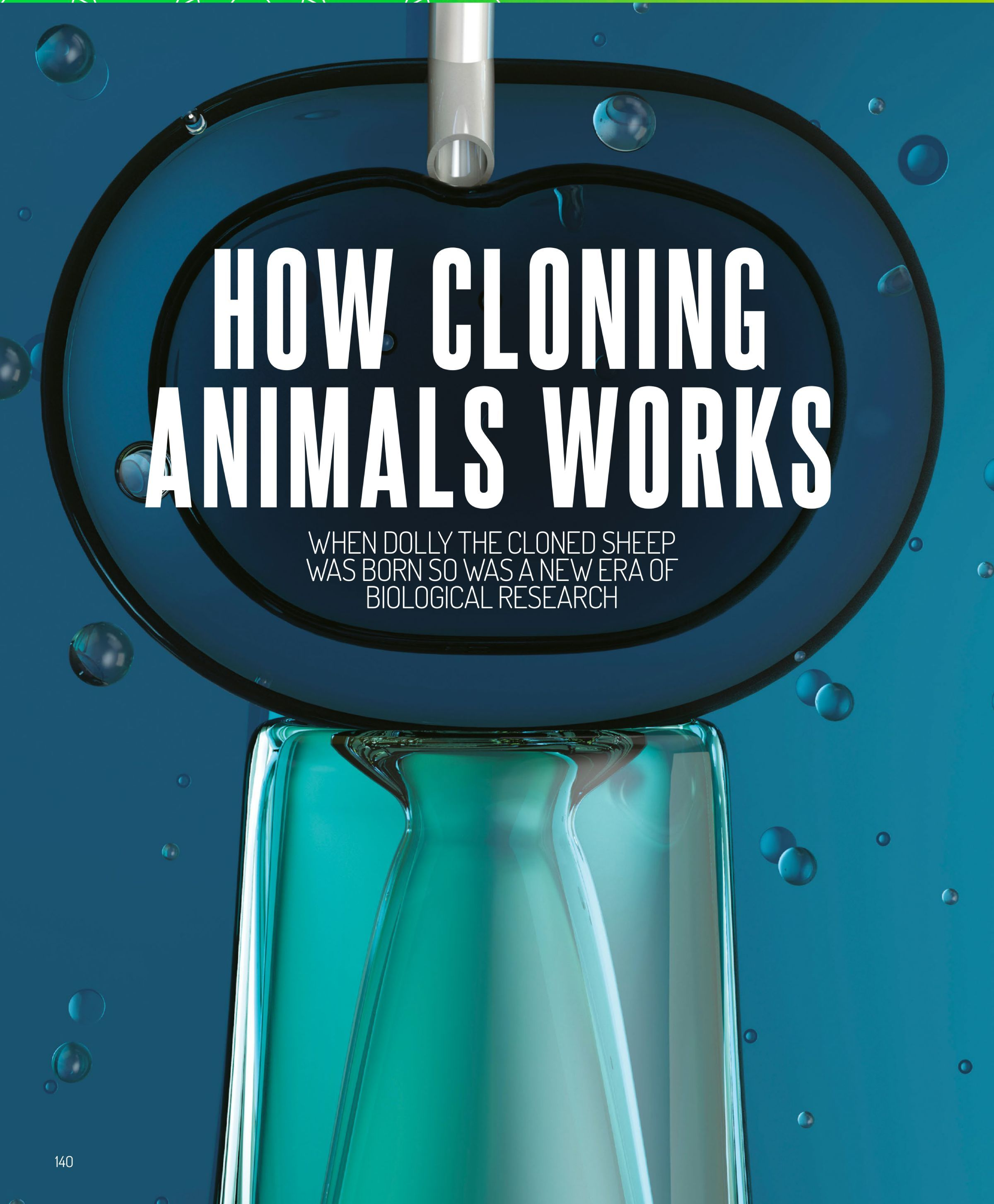


HOW CLONING ANIMALS WORKS

WHEN DOLLY THE CLONED SHEEP WAS BORN SO WAS A NEW ERA OF BIOLOGICAL RESEARCH

She was born into the world like any other sheep – tiny, fluffy and bleating. But Dolly wasn't the same as any other sheep. Or rather, her uniqueness was that she was like just one other sheep. In fact, she was identical to one other sheep. Dolly was a clone.

Clones are organisms, or cells, that are genetically identical to their parent, and they have existed in nature for millions of years. Single-celled organisms and plants can produce genetically identical offspring and natural clones, for example identical twins, occur in humans and other mammals. These natural clones have almost identical DNA. However, animal cloning has been experimented with for over 100 years, starting with more basic animals like salamanders and working up to complex mammals like sheep and cows.

DOUBLE TROUBLE: CLONING METHODS

There are two main methods of cloning animals: somatic cell nuclear transfer (SCNT) and embryo splitting. It was the SCNT method that was used to produce Dolly the sheep. Both methods are forms of 'reproductive cloning', a type of artifical cloning of which gene cloning and therapeutic cloning are also a part of.

○ Two cloned beagles, Magic and Stem, were born at the National Seoul University in January 2009 in Seoul, South Korea

"Animal cloning has been experimented with for over 100 years, starting with more basic animals like salamanders"

REPRODUCTIVE CLONING

SCNT cloning starts with finding a suitable nucleus donor. These can be obtained directly from the animal or they can be grown in a laboratory. They are usually skin cells, which have a relatively long lifespan and can tolerate being frozen. The other cell that needs to be obtained for the cloning procedure is an egg cell. The egg cell is enucleated – a process that involves sucking out the nucleus by using a tiny needle. When the cell has been enucleated there is no DNA left behind, but it remains filled with cytoplasm. The nucleus donor cell is enucleated in the same way, but instead of being discarded the lone nucleus is injected into the egg cell. An electric shock is applied, which triggers it to start dividing. If everything goes well the embryo is implanted into a surrogate. The cells divide normally, and a few months later a healthy clone is born. So far, there is no evidence that the process is at all detrimental to the clone. Dolly was able to reproduce and had healthy offspring, which suggests even her fertility was not impacted by the way she came into life.

THERAPEUTIC CLONING

Therapeutic cloning uses the same methods, right up until the point of electric shock. The

ACHIEVEMENTS IN CLONING HISTORY

THE BREAKTHROUGH MOMENTS IN SCIENTIFIC HISTORY THAT ADVANCED THE FIELD OF CLONING

1938
Hans Spemann proposes a "fantastical experiment" to transfer one cell's nucleus into an egg without a nucleus, the basic method that would eventually be used in cloning.

1952
Robert Briggs and Thomas King successfully transfer the nucleus from an early tadpole embryo into an enucleated frog egg.

1984
Steen Willadsen clones a sheep from an embryonic cell in a technique known as nuclear transfer.

1996
Dolly the sheep – the first mammal ever to be cloned from an adult body cell – is born.

2001
Two animals – a mouflon sheep and a gaur (Indian bison) – are cloned as part of an effort to save these species.

2003
Researchers successfully clone the first extinct animal, a Spanish mountain goat called the bucardo, but the clone died minutes after it was born.

2013
Human embryos are cloned for the first time to produce embryonic stem cells with the hope they may go on to treat diseases.

© Getty

THE LIFE OF DOLLY THE SHEEP

Dolly was born on 5 July 1996 at The Roslin Institute in Scotland. Her birth was a result of an experiment to develop genetically modified livestock. She had three mothers: a Finn-Dorset provided the DNA, a Scottish Blackface provided the egg and a third, a Scottish Blackface, was impregnated with the embryo. 148 days later, the surrogate ewe gave birth to Dolly. She was the sole surviving adult from 277 cloning attempts.

Dolly went on to have six healthy lambs, all conceived naturally. She died at the age of six from a disease unrelated to her being a clone, but her life encouraged scientists to continue experiments with other animals. Since then pigs, cats, cows, horses and even camels have been successfully cloned.

○ The Seoul National University and RNL Bio Company offers clients a service to clone their dead pets

donor cell, however, belongs to a cell from a patient in need of stem cells. After the fused cells have divided several times it becomes a pre-embryo ball of cells known as a blastocyst. A blastocyst has an outer and inner layer, and within the inner layer are the prized stem cells. While most cells are specialised to a specific job (i.e. neuron, muscle cell etc.) stem cells have the potential to develop into any type of cell. The harvested stem cells are infused into a patient and, under the right conditions, start functioning where needed.

EMBRYO SPLITTING

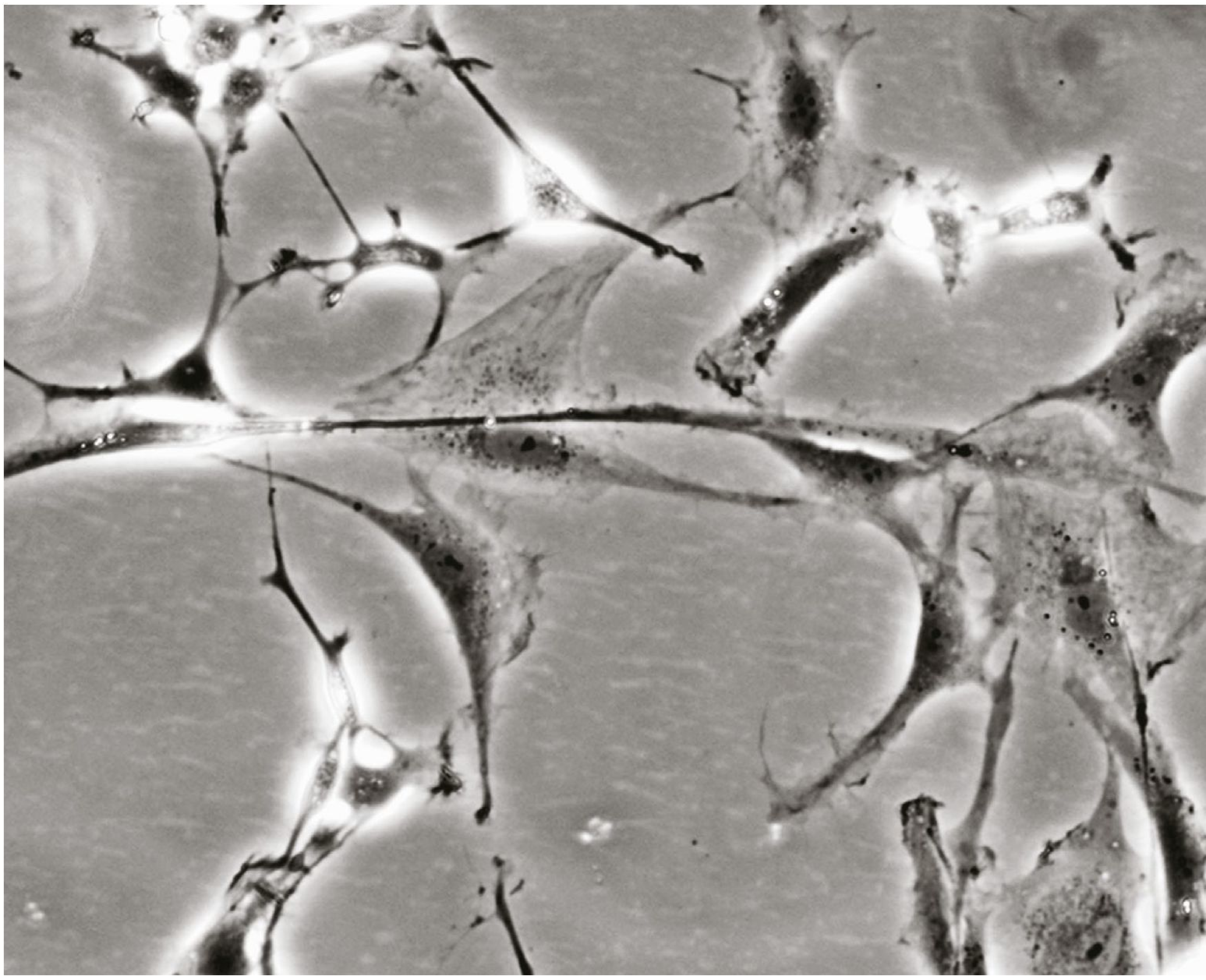
The simplest form of artificial cloning, this method begins with the formation of a zygote. This zygote divides and eventually the embryonic cells can be separated. Each separated cell continues growing and can be implanted into a surrogate. The implanted cells are identical as they were originally formed from the same embryo. This process is similar to that of the development in identical twins but has a limited potential.

CAN WE CLONE HUMANS?

Undoubtedly, cloning is a powerful biological technology. Scientists have been able to use the technique to breed endangered species and resurrect extinct animals. There has even been talk of bringing back the woolly mammoth after the discovery of preserved soft-tissue remains of these prehistoric giants. Yet, while laboratories are researching and developing therapeutic cloning using human tissue, there have been no actual human clones created to date. This is partly due to the ethical problem of bringing cloned individuals into existence without fully knowing if the method is safe or what the impact might be on the cloned human's life. Other concerns include the fact that reproductive cloning could be prone to wide-scale abuse, such as cloned humans being used for organ and tissue harvesting.

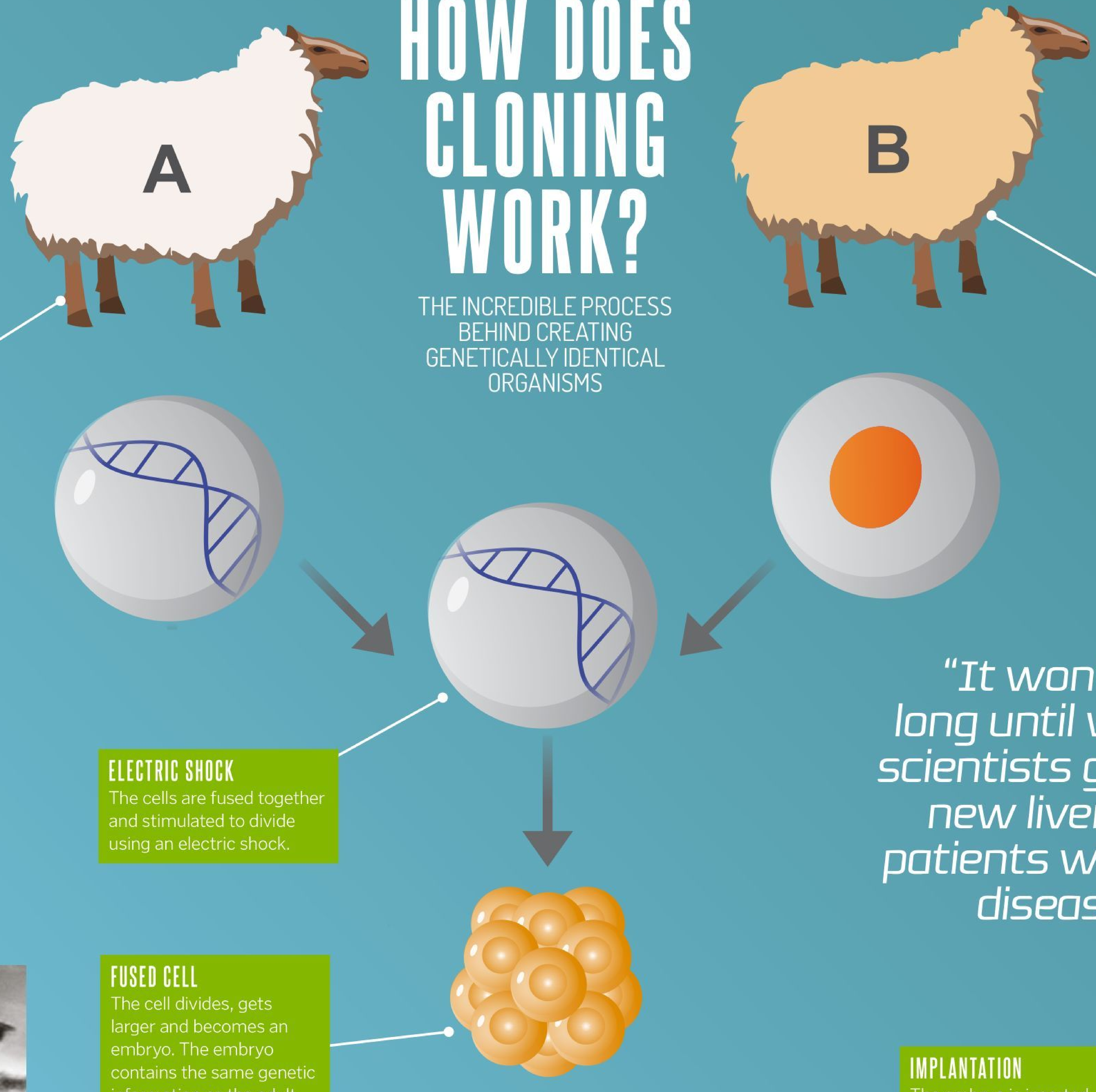
WHAT'S THE POINT?

Cloning is expensive, time-consuming and has a very low success rate. However, developing these methods has been vital to our understanding of human developmental biology and has provided new treatment options in medicine. It is hoped that soon patients with an organ disease or failure will no longer have to risk their body rejecting their new transplant. Instead, they will be able to replace the organ with one that is genetically identical but without the wear and tear. It won't be long until we see scientists growing new livers for patients with liver disease, new hearts for transplants and even new brain neurons for people suffering from brain injuries – all perfectly genetically identical to the patient.



HOW DOES CLONING WORK?

THE INCREDIBLE PROCESS BEHIND CREATING GENETICALLY IDENTICAL ORGANISMS

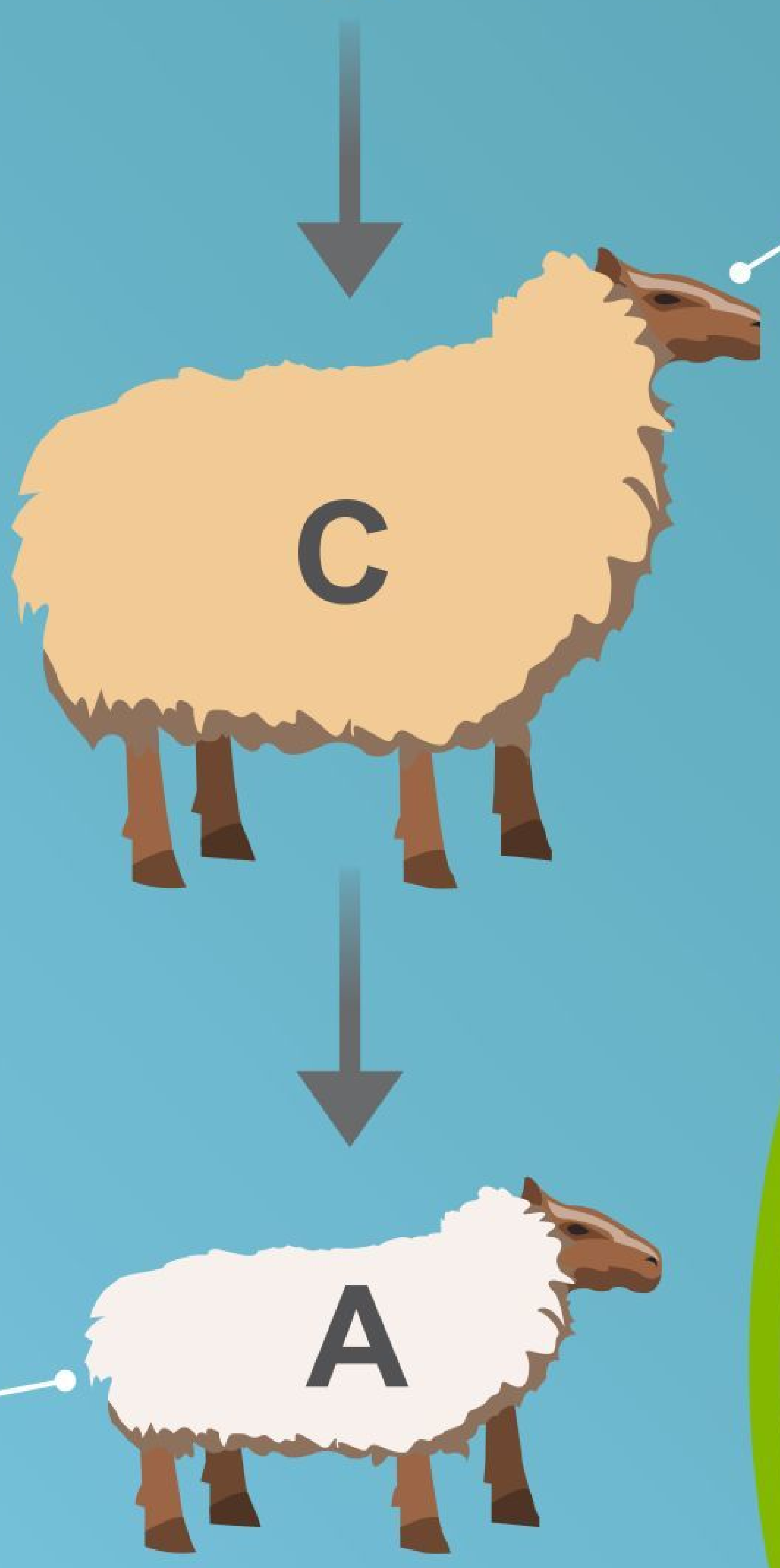


DONOR MAMMARY CELLS
A donor cell has its nucleus removed and the rest of the cell is discarded.

ADULT DONOR CELLS
An enucleated egg cell from another donor is injected with the extracted nucleus.

ELECTRIC SHOCK
The cells are fused together and stimulated to divide using an electric shock.

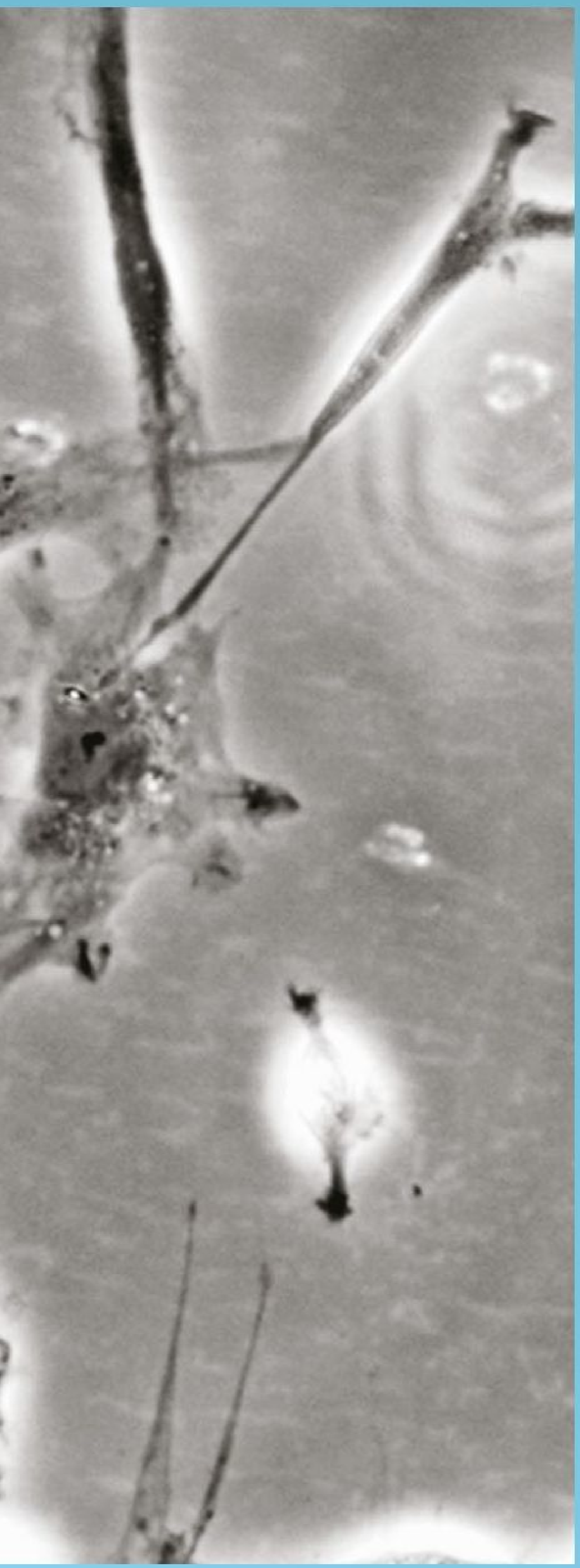
FUSED CELL
The cell divides, gets larger and becomes an embryo. The embryo contains the same genetic information as the adult mammary cell.



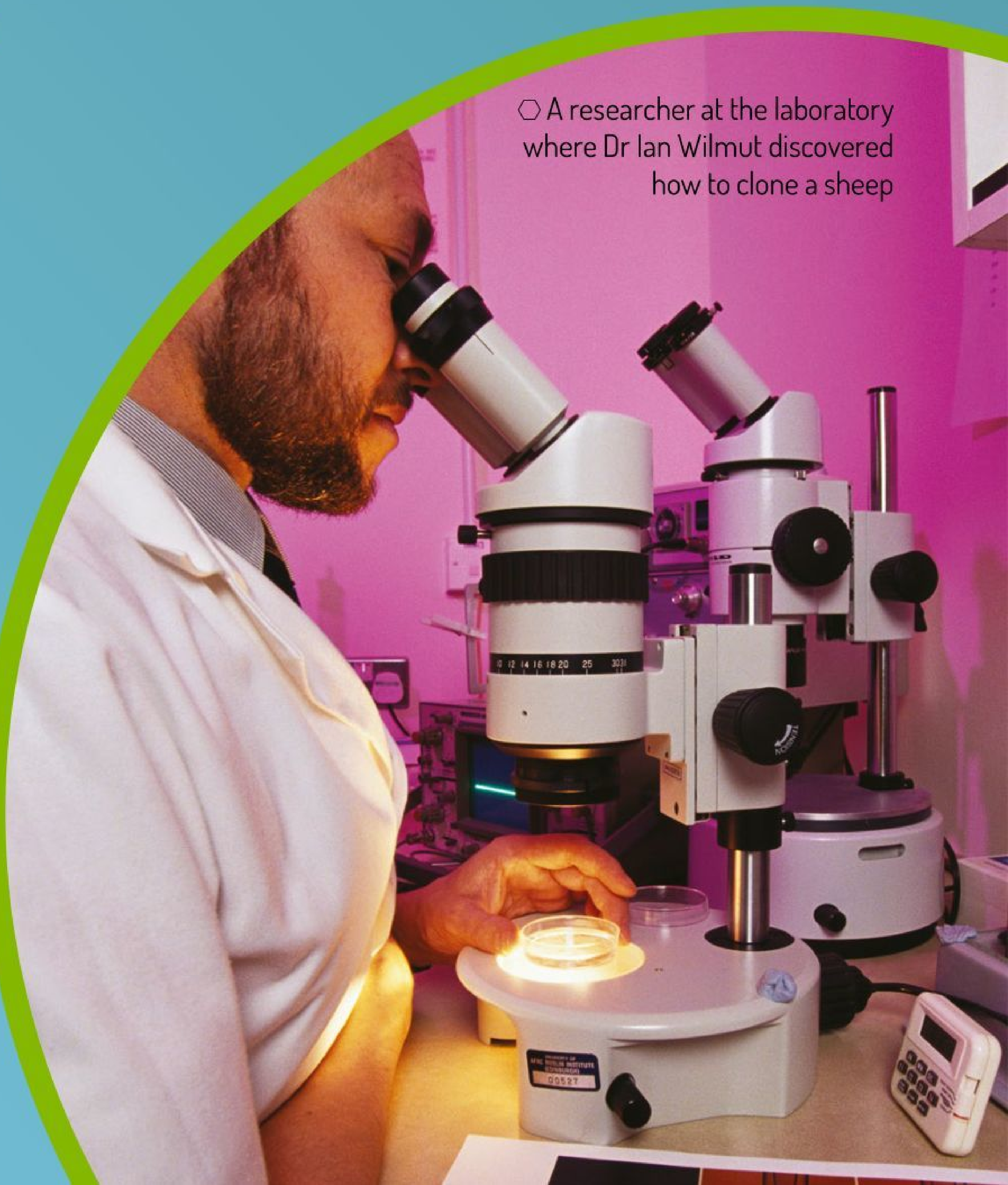
IMPLANTATION
The embryo is inserted into the uterus of a surrogate mother.

CLONE IS BORN
The embryo develops normally and is born.

> *"It won't be long until we see scientists growing new livers for patients with liver disease"*



⬡ Colonies of neural stem cells are capable of differentiating into any cell of the nervous system



⬡ A researcher at the laboratory where Dr Ian Wilmut discovered how to clone a sheep

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HOW WE'LL CURE CANCER

FIND OUT HOW UNDERSTANDING ONE OF HUMANITY'S OLDEST ADVERSARIES COULD SOON LEAD TO A CURE

Cancer has been around longer than we have. Traces have been found in 70 million-year-old dinosaur bones, in a 120,000-year-old Neanderthal rib, and in a human skeleton dating back to 1200 BCE. And almost every animal, even sharks and naked mole rats, can get the disease.

It was once untreatable. Ancient Roman doctor Celsus wrote, "After excision, even when a scar has formed, none the less the disease has returned." Even if the tumours were removed, they kept coming back, but in ancient times we didn't fully understand exactly what we were up against.

By the 17th century, physicians were pointing the finger at a straw-coloured liquid called lymph, which passes through the body in channels that run alongside the blood vessels. And by the mid-1800s, it became clear that cancers were actually made from cells.

Realising that cancer spread from the original tumour, 19th-century surgeons, with the help of new anaesthetics, started removing more tissue and nearby lymph nodes. Then, at the start of the 20th century, radiotherapy became available to treat irremovable cancers. Nitrogen mustards then became the first chemotherapy drugs after WWI.

Then a massive breakthrough was made. In 1953, James Watson and Francis Crick deciphered the structure of DNA, opening the door to a new era of genetic science. We now know that tumours are made of our own cells but their genes have gone wrong. They change constantly, they evolve to escape treatments, and they hide and spread undetected. And the more we learn, the more we are unravelling their weaknesses.

A century ago a cure for cancer would have been unthinkable, but as research continues survival is rising, and there are many more discoveries yet to be made.

> "Watson and Crick deciphered the structure of DNA"

○ Damage builds up in our DNA over time, making cancer more common in older people

○ Lung cancer is the most common type of cancer across the world

CANCER STATISTICS

14 MILLION
PEOPLE WERE DIAGNOSED WITH CANCER IN 2012

22%
OF CANCER DEATHS ARE CAUSED BY SMOKING

8.2 MILLION
PEOPLE DIED FROM CANCER IN 2012

70%
OF CANCERS HAPPEN IN LOW AND MIDDLE INCOME COUNTRIES

CANCER IS THE SECOND HIGHEST CAUSE OF DEATH IN THE WORLD

UP TO HALF OF ALL TYPES OF CANCER CAN BE PREVENTED BY LIFESTYLE CHANGES

LUNG CANCER IS THE MOST COMMON WORLDWIDE, FOLLOWED BY BREAST AND COLON

THE UK HAS THE 23RD HIGHEST CANCER RATE IN THE WORLD

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WHAT IS CANCER?

THE FIRST STEP TO FINDING A CURE IS UNDERSTANDING EXACTLY WHAT WE'RE UP AGAINST

You're made up of an estimated 37.2 trillion cells, each containing an entire copy of your DNA, which consists of 23 pairs of chromosomes and 21,000 genes, written in combinations of four chemical 'letters': A, C, G and T.

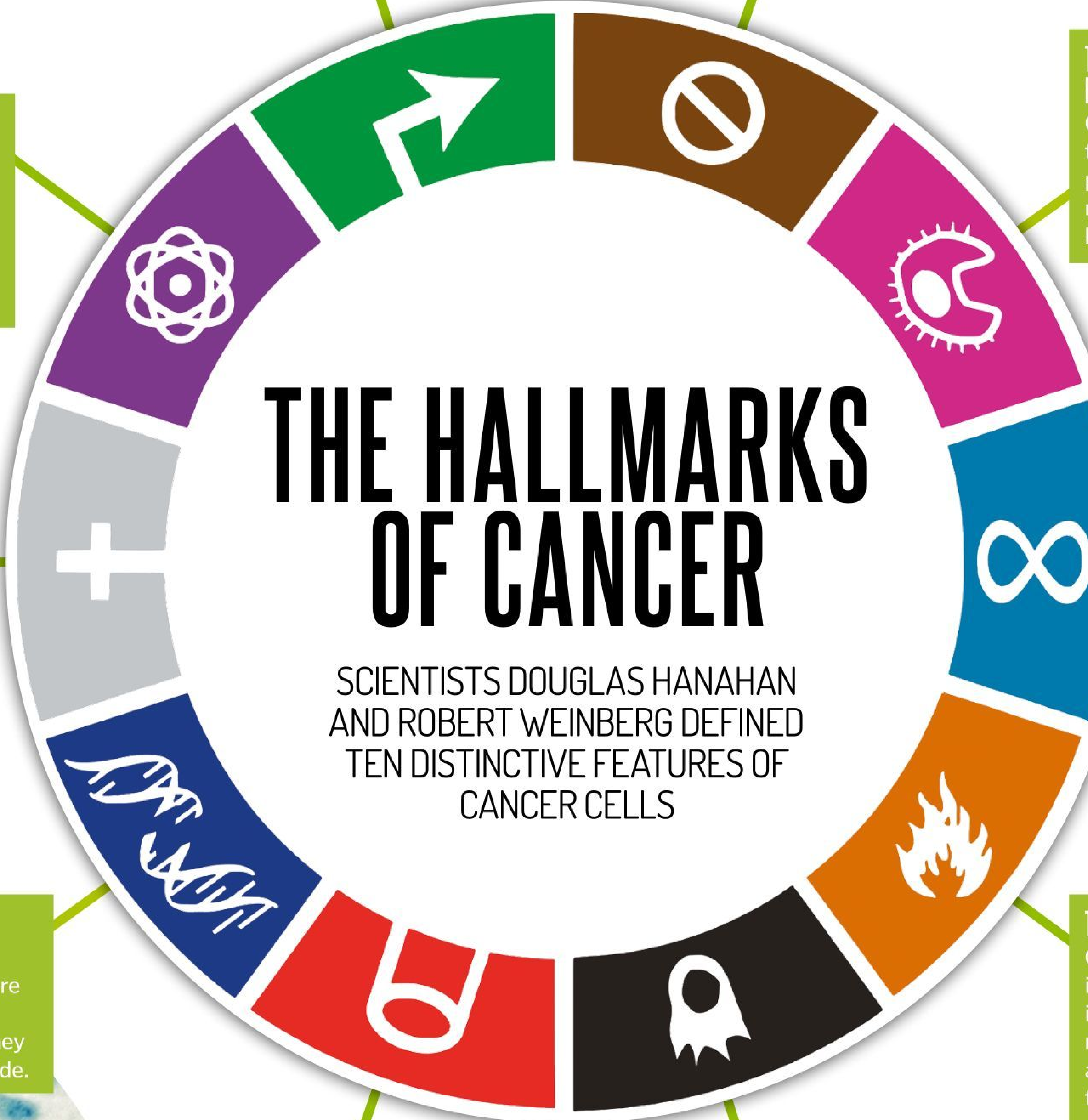
The full human DNA sequence contains around 3 billion letters, and the genes are arranged into three-letter 'words' called codons. Each word corresponds to a molecular building block called an amino acid and, when genes are read in order, the words in a gene provide the recipe to build a protein. Proteins are crucial for everything that a cell does, from making energy to deciding when to divide to communicating with its neighbours. But in cancer cells vital genes contain mistakes, changing their proteins and altering the way that they behave.

It takes lots of genetic mistakes to turn a healthy cell into a cancer cell, and they tend to build up over time. A few people inherit genetic faults from their parents, but most occur as we get older. Sunlight, alcohol, radiation and smoking, for example, can all cause harm to our genetic code. But even people with the healthiest lifestyles accumulate genetic faults.

Cells divide for growth and repair, making copies of themselves to replace old cells or to heal wounds. In order to do this, a cell must first duplicate all 3 billion letters of its DNA, and doing this without making a single mistake is a virtually impossible task.

The copied code is scanned for errors, and mistakes are usually fixed before the cell

> "Cancer cells keep making copies of themselves with more mistakes"



THE HALLMARKS OF CANCER

SCIENTISTS DOUGLAS HANAHAN AND ROBERT WEINBERG DEFINED TEN DISTINCTIVE FEATURES OF CANCER CELLS

THEY KEEP GROWING
Cells normally wait for a signal to divide, but cancer cells make their own growth signals.

THEY DON'T STOP WHEN TOLD
Cancer cells ignore signals telling them to stop dividing.

THEY AVOID WHITE BLOOD CELLS
Cancer cells hide from the immune system, preventing the body's natural defences from killing them.

THEY ARE IMMORTAL
Normal cells stop dividing when they become old, but cancer cells keep on replicating indefinitely.

THEY CREATE INFLAMMATION
Cancer cells hijack immune cells, using inflammation that would normally help to fight against an infection to their own advantage.

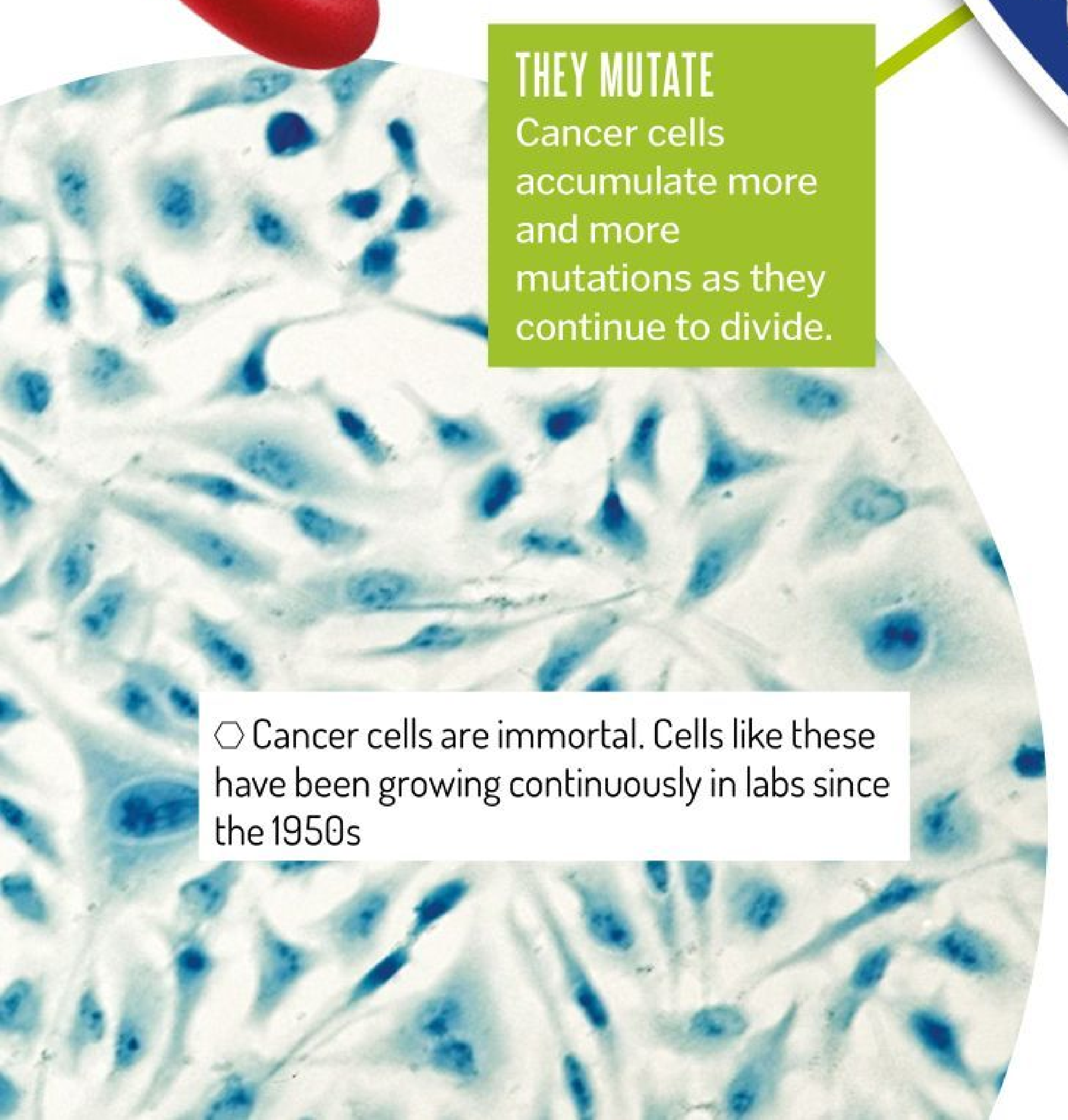
THEY SPREAD
Cancer cells can spread around the body, creating more tumours in other places.

THEY SET UP FUEL LINES
As tumours grow, they get more oxygen and nutrients by encouraging new blood vessels to form.

THEY MUTATE
Cancer cells accumulate more and more mutations as they continue to divide.

THEY RESIST DEATH
Healthy cells self-destruct when they are damaged, but cancer cells turn this safety switch off.

THEY CHANGE THEIR METABOLISM
Cancer cells reprogram their metabolism to keep dividing under conditions that would normally kill other cells.



○ Cancer cells are immortal. Cells like these have been growing continuously in labs since the 1950s

divides, but sometimes errors slip through and over time they start to build up.

Just as changing the letters in a book would make the words unreadable, changing the letters in the genetic code makes it hard for the cell to make sense of its genes. If letters are changed, deleted, added or moved around, it can completely change the meaning of the genetic words, which in turn changes the proteins that the cell makes.

Built-in safety mechanisms normally tell a cell to self-destruct if it has too many genetic errors, allowing a new, healthy cell to take its place. But sometimes damaged cells slip through the net, failing to repair themselves and resisting the signals to die.

Cancer cells tend to have errors in genes known as 'oncogenes' or 'tumour suppressor genes'. Oncogenes are normally responsible for telling healthy cells to divide, helping with growth and wound repair, but mutations in cancer can cause them to become permanently switched on. Tumour suppressor genes, on the other hand, tell cells to stop dividing once growth or repair is completed, and errors in these genes can cause them to turn off. The result is that the damaged cells divide and divide and divide, piling up on top of each other to form a tumour.

With their safety systems switched off and nothing to tell them to stop, cancer cells keep making copies of themselves with more mistakes in their genetic code, and this leads to Darwinian evolution at a rapid speed. Just as if a wild animal has a beneficial genetic trait it will be more likely to reproduce, if a cancer cell has a beneficial trait it will be more likely to survive.

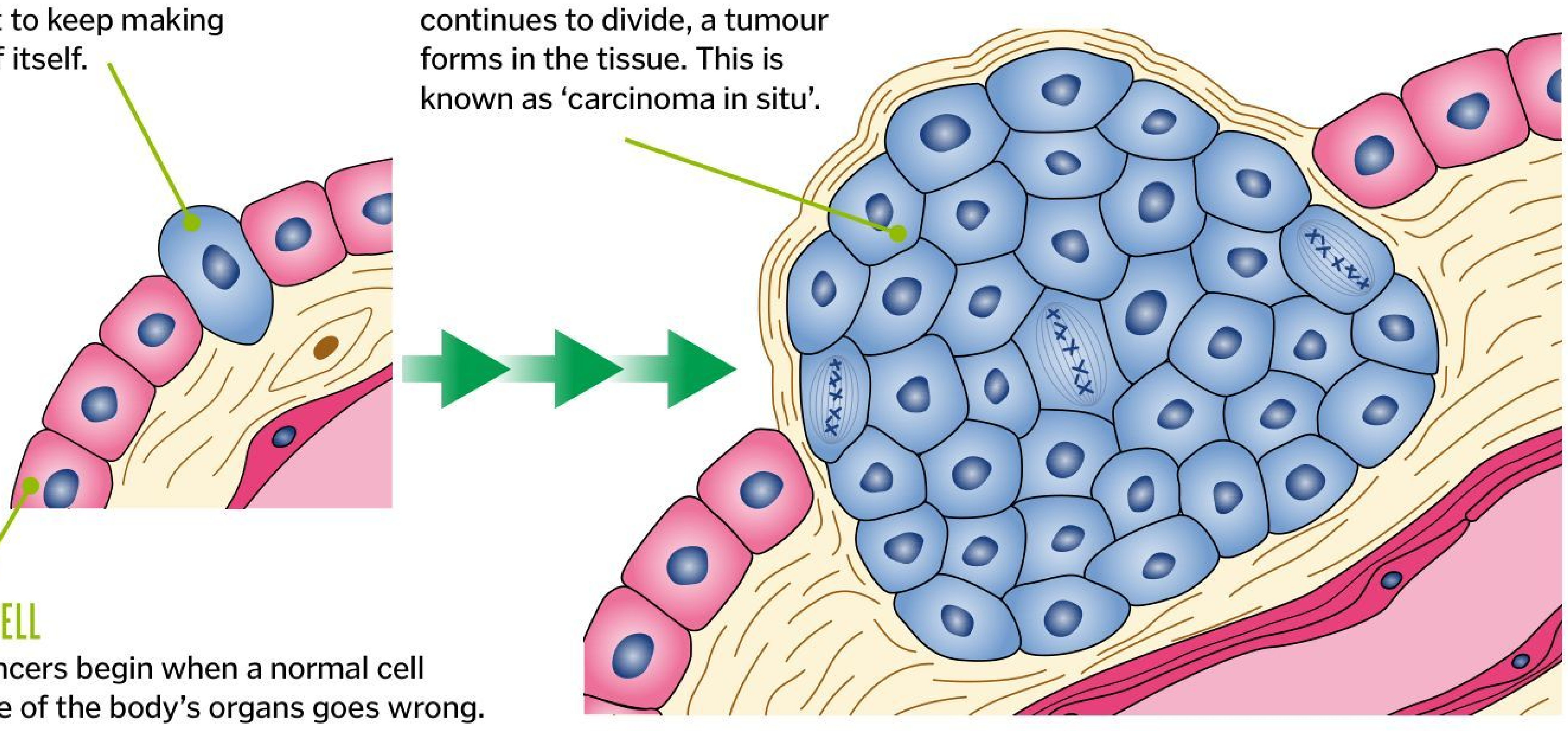
Cancer cells forget what they are supposed to be doing and gain new abilities, developing traits that allow them to hide from the immune system, survive on less oxygen, and even evade chemotherapy. But, most dangerous of all, they gain the ability to move through the body, spreading to distant places via the blood or lymphatic systems and making new tumours elsewhere. But the more we understand about how cancer works, the better we are becoming at treating it.

HOW CANCER STARTS

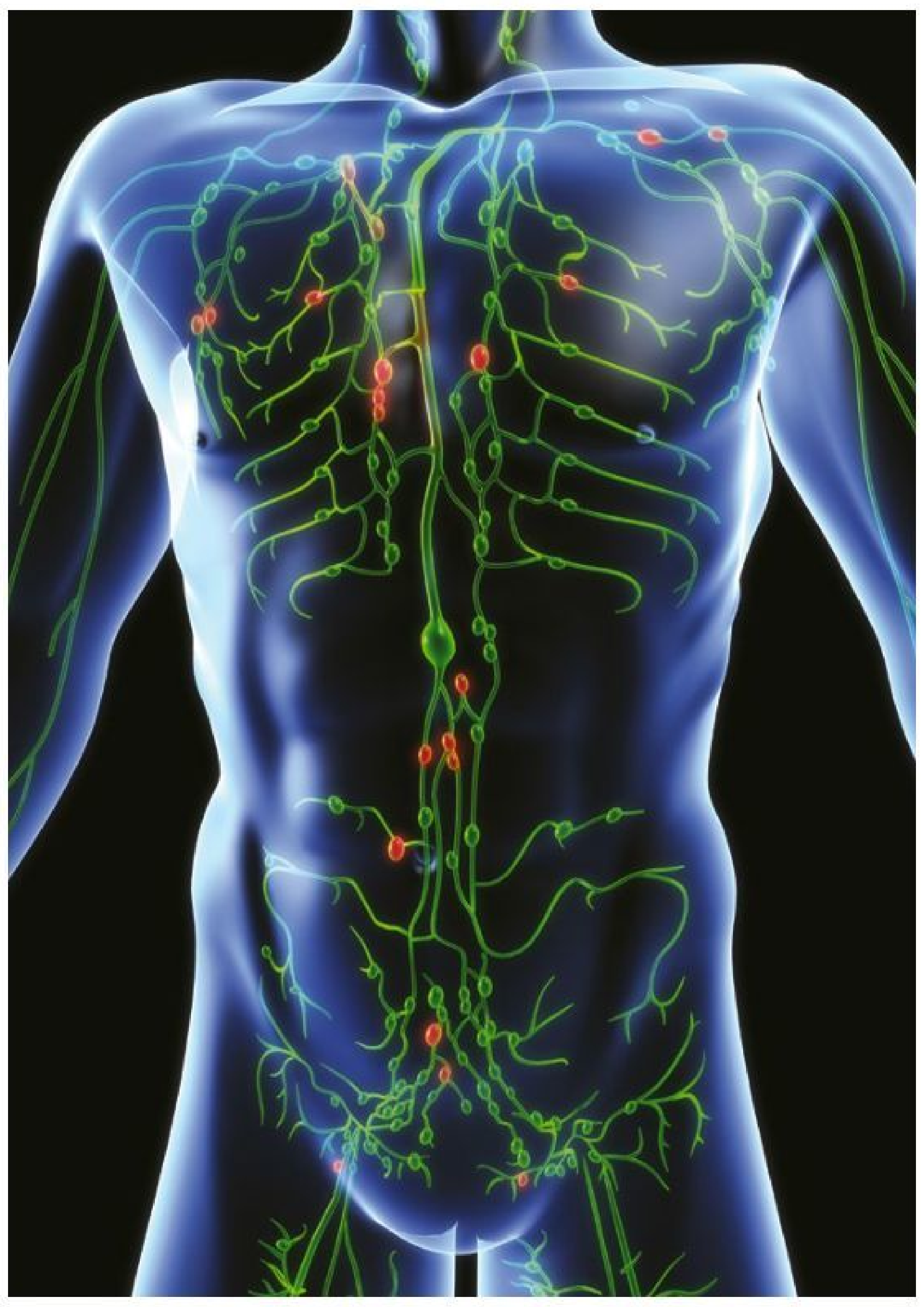
CANCER BEGINS WITH A SINGLE MUTATED CELL THAT DIVIDES AND SPREADS

CANCER CELL
Genetic errors inside the cell tell it to keep making copies of itself.

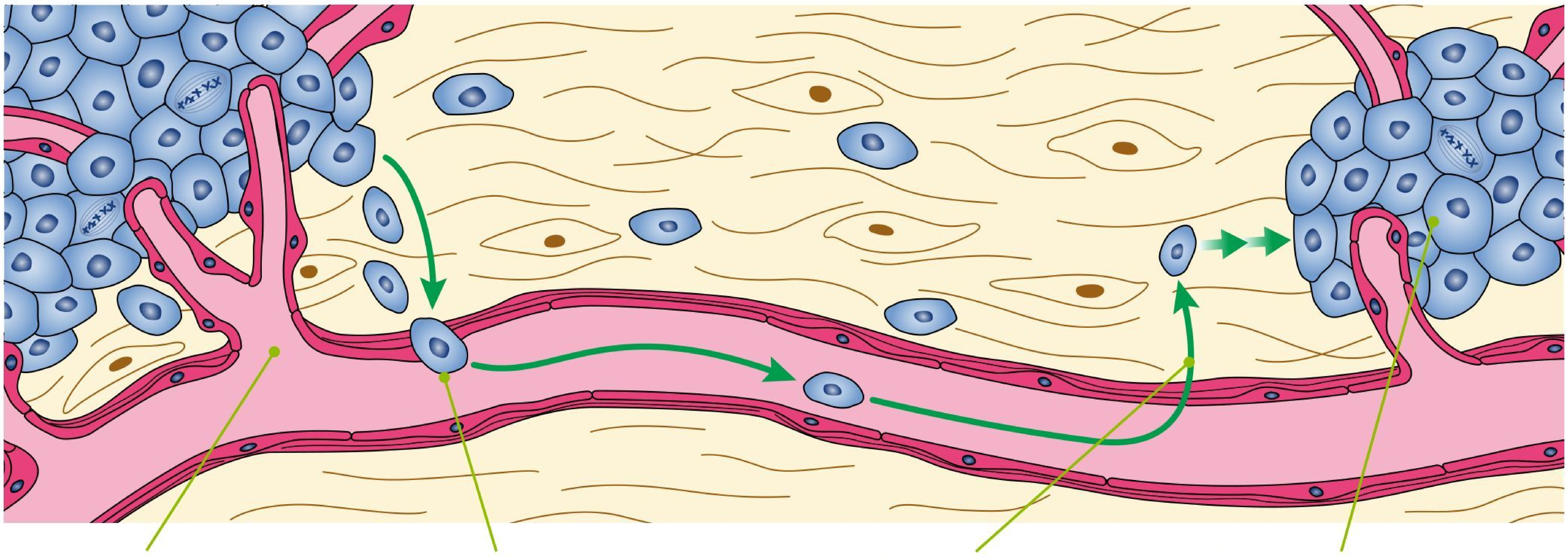
TUMOUR
As the abnormal cell continues to divide, a tumour forms in the tissue. This is known as 'carcinoma in situ'.



NORMAL CELL
Most cancers begin when a normal cell lining one of the body's organs goes wrong.



○ Cancer cells can use the lymphatic system to spread around the body



BLOOD VESSELS
To keep growing the tumour needs a blood supply, so it encourages the formation of new blood vessels.

DISTANT SPREAD
Cells start to break away from the main tumour, entering the lymphatic system and the blood vessels and spreading around the body.

LOCAL SPREAD
Eventually, the tumour starts to invade the local tissue, growing down into the connective tissue below.

SECONDARY TUMOUR
Cancer cells become lodged in different tissues and continue growing, forming more tumours known as 'secondaries' or 'metastases'.

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TREATING CANCER

THERE ARE THREE MAJOR TYPES OF CANCER TREATMENT: SURGERY, RADIOTHERAPY AND CHEMOTHERAPY

CHEMOTHERAPY

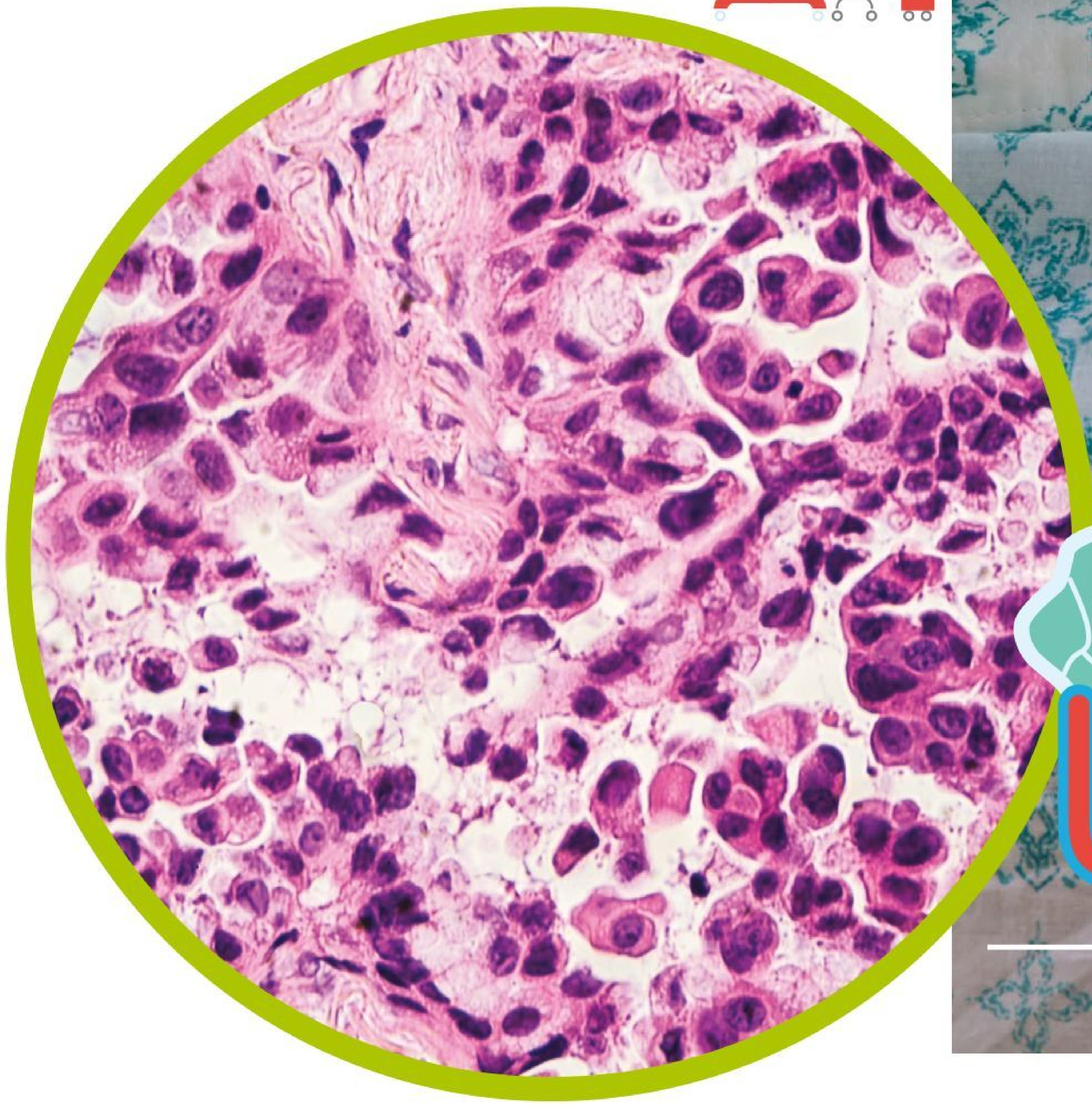
The first chemotherapy drug was developed using mustard gas, a chemical weapon used during WWI. Scientists had noticed that the poison killed the fast-dividing cells of the bone marrow, and so they adjusted the weapon to make nitrogen mustard, a treatment that could kill rapidly replicating cancer cells.

Nitrogen mustard belongs to a group of drugs known as alkylating agents, which work by adding chemical units called alkyl groups to DNA. These interfere with the double helix structure, causing the genetic code to break apart.

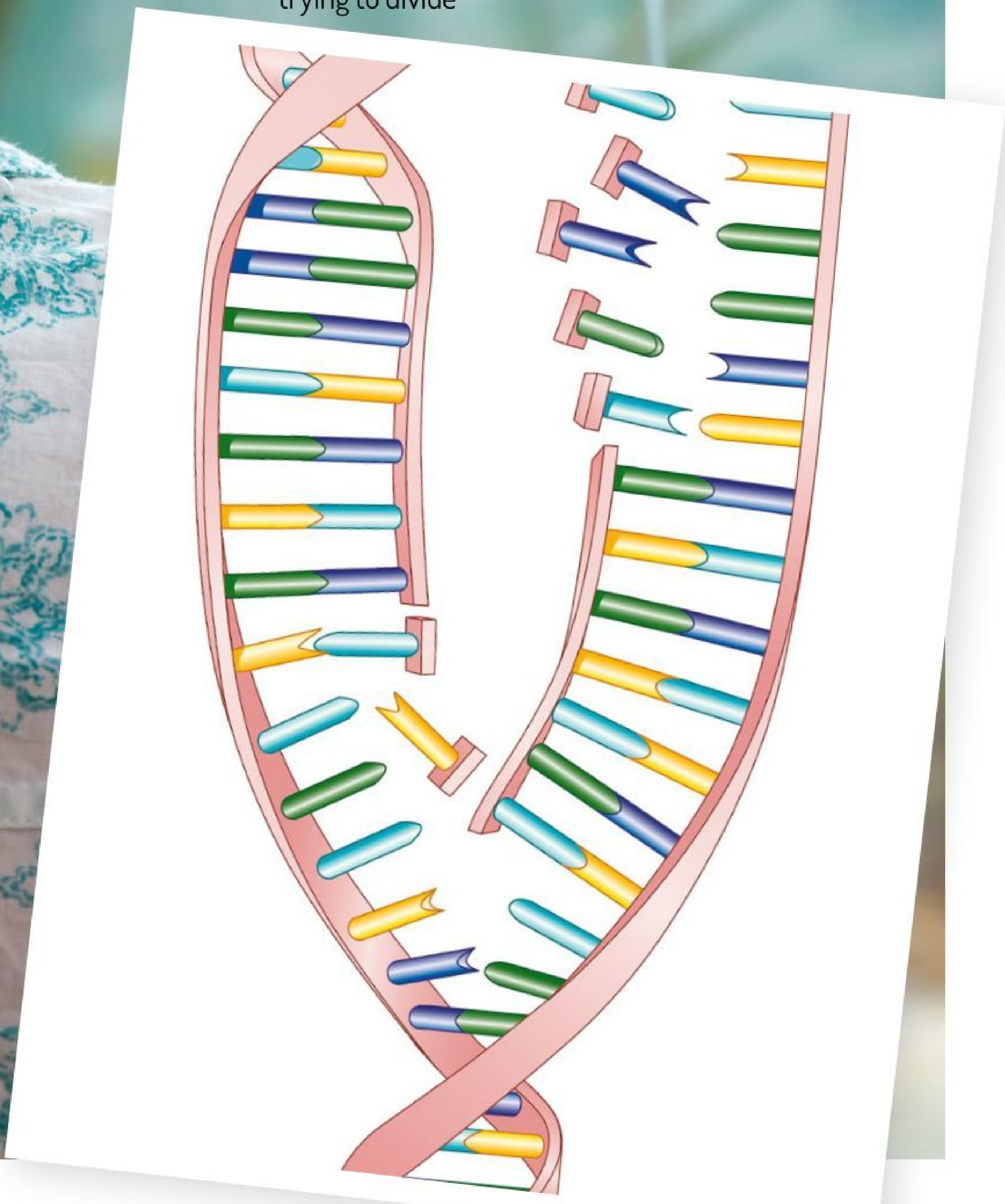
Other chemotherapies work in similar ways. Heavy metals cross-link DNA, preventing it from being read. Topoisomerase inhibitors stop the DNA helix from unwinding, and antimetabolites work by mimicking molecules involved in copying DNA, stopping the new sequence from being made. Anti-microtubule, or spindle poisons, stop cells from splitting apart, and cytotoxic antibiotics stick to the DNA helix, prevent unwinding, link different strands of DNA together or break DNA into fragments.

These treatments are particularly harmful to cells that are trying to make copies of themselves because they target DNA replication and cell division. This is good for catching fast-dividing cancer cells, but it isn't perfect. Cancer cells aren't always dividing, so some cells manage to escape the treatment, and lots of healthy cells also divide rapidly, too. Hair, skin and bone marrow (which makes blood cells) are all damaged by chemotherapy, leading to side-effects like hair loss, sickness and a weakened immune system.

⬡ Pathologists examine images like these to diagnose cancer. This lung tissue should be full of holes



⬡ Chemotherapies harm cells that are trying to divide



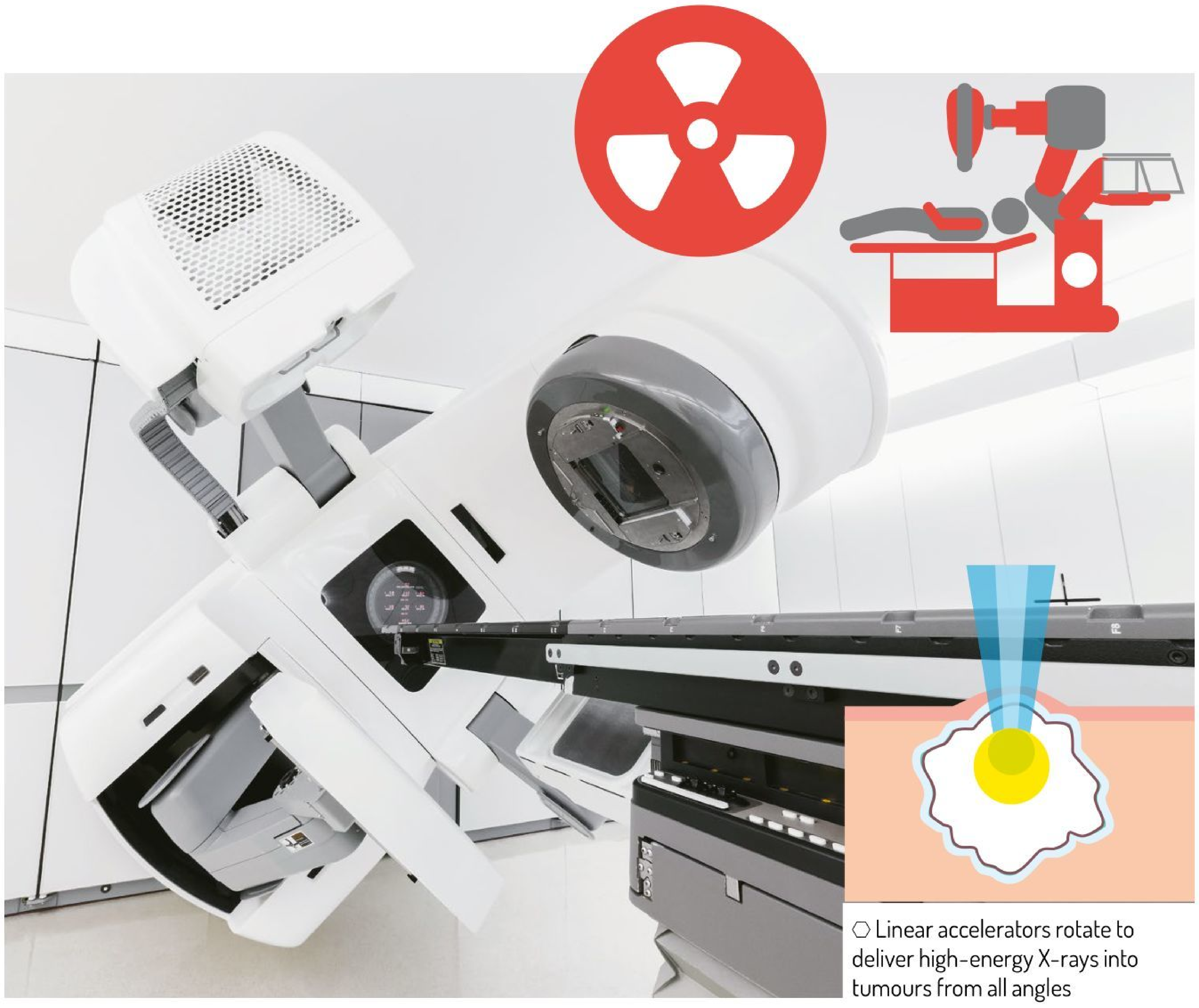
RADIOTHERAPY

Radiotherapy was developed in the early 20th century and works by bombarding cancer cells with radiation. When the water molecules inside the cells are hit they split apart in a process called radiolysis. This makes highly reactive free radicals with an unpaired electron that attacks bonds belonging to other molecules, setting off a chain reaction that damages DNA.

Radiotherapy causes both strands of the DNA to break close together, a lesion known as a 'double-strand' break. This makes the helix unstable and it starts to unwind. Cells can repair a bit of this kind of damage, but the more radiation they receive, the more likely they are to die.

The most common way to deliver radiotherapy is by using a linear accelerator (LINAC). It uses microwaves to make electrons, which hit a heavy metal to make X-rays. CT or MRI scans are used to pinpoint the exact location of the tumour inside the body, and the X-rays are then shaped to fit the outline of the tumour. This is done by blocking part of the beam using sheets of metal known as a multileaf collimator.

X-rays go all the way through the body, so the machine rotates to deliver beams from all angles, giving the maximum dose where the beams cross over at the site of the tumour, minimising the amount of radiation received by the surrounding healthy tissue.



○ Linear accelerators rotate to deliver high-energy X-rays into tumours from all angles

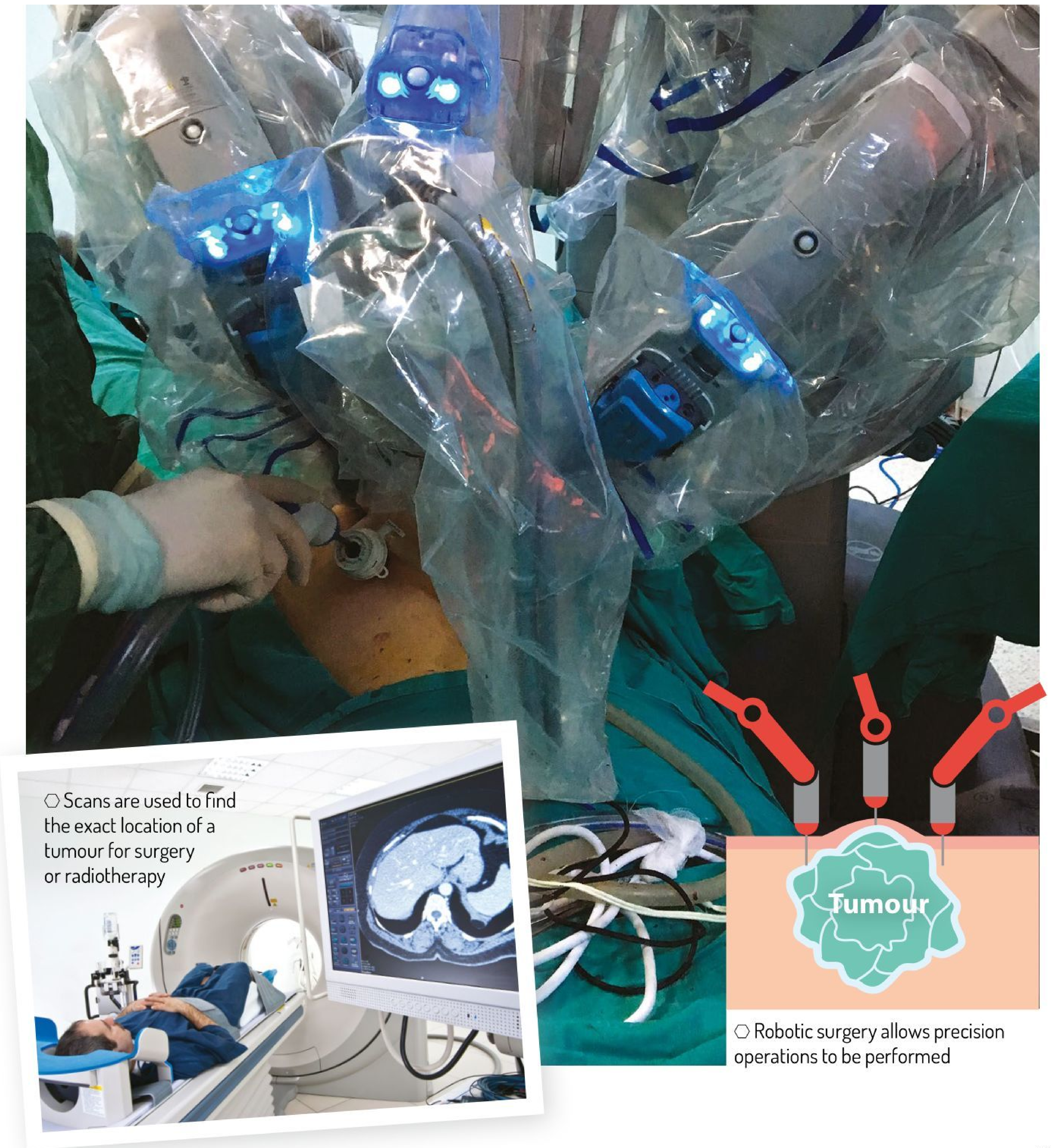
SURGERY

Surgery is one of the oldest and most effective cancer treatments. If the cancer hasn't spread, surgeons take out the whole tumour and some of the surrounding area in case there are any cells that can't be seen. Nearby lymph nodes may also be removed as these are often the first place a cancer will spread to.

If the whole tumour cannot be removed, surgery can also be used for 'debulking', where as much of the tumour is removed as possible so the rest can be treated with chemotherapy or radiotherapy. Surgery can also be palliative, relieving symptoms when cancer cannot be cured.

Not all lumps are tumours and not all tumours are cancer, so surgery is often used for cancer diagnosis, too. A small sample of tissue, known as a biopsy, is removed and either frozen solid or embedded in wax so that it can be thinly sliced. These slices are stained so that a pathologist can examine the structure of the cells and tissue.

Cancer cells look different under a microscope, creating disorganised structures in normally orderly tissues, and they also display specific molecular or genetic markers that single them out. These not only help with a cancer diagnosis but can also be used to determine the type of cancer, how advanced it is and the best form of treatment to use against it.



○ Scans are used to find the exact location of a tumour for surgery or radiotherapy

○ Robotic surgery allows precision operations to be performed

THE FUTURE OF CANCER TREATMENT

THE MORE WE LEARN ABOUT CANCER, THE BETTER WE ARE ABLE TO TARGET ITS WEAKNESSES

In the UK, overall cancer survival is now at 50 per cent, and ten-year survival for testicular cancer has reached an impressive 98 per cent. But there's still a way to go. There are hundreds of different types of cancer, and even patients with the same cancer type have subtle differences in their tumours that change their response to treatment. Cancers can become resistant to chemotherapy and radiotherapy, and many treatments also harm healthy cells, causing side-effects that limit their use.

Until recently, most cancer treatments have focused on one thing: cell division. Both radiotherapy and chemotherapy hit rapidly dividing cells, damaging their DNA as they try to replicate, causing them to die. But cancer has lots of other weaknesses and scientists are attacking from all angles, using the latest tech to reveal their genetic and molecular differences.

One tactic is to cut cancer's fuel lines. As tumours grow and cells pile on top of one another, oxygen levels drop and the cancer cells encourage new blood vessel cells to break down tissue and migrate in. Blocking this process could stop tumour growth in its tracks.

Another option is to use the immune system, helping our own cells to see cancer cells and destroy them. Techniques being trialled include using molecules to block the interaction between cancer cells and immune cells, preventing the tumour from switching the immune system off, and genetically engineering immune cells to supercharge their ability to seek and destroy cancer cells.

Immune molecules called antibodies are also being transformed into highly targeted cancer treatments that should leave healthy cells unharmed. They can be made to stick specifically to a single molecule, blocking the chemical signals that tumours need to survive or attaching directly to the cancer cells. They can even be linked to chemotherapy or radiotherapy molecules, delivering a double hit of toxin and immune attack.

Researchers are also working on genetically modifying viruses to infect and kill cancer cells, delivering drugs into cancer cells using nanoparticles and designing small molecules to interfere with the crucial molecular machinery that cancer cells use to survive.

It's very unlikely that there will ever be a single cancer cure, but the more we learn, the more targeted treatments will become, killing cancer cells more effectively and leaving healthy cells unharmed.

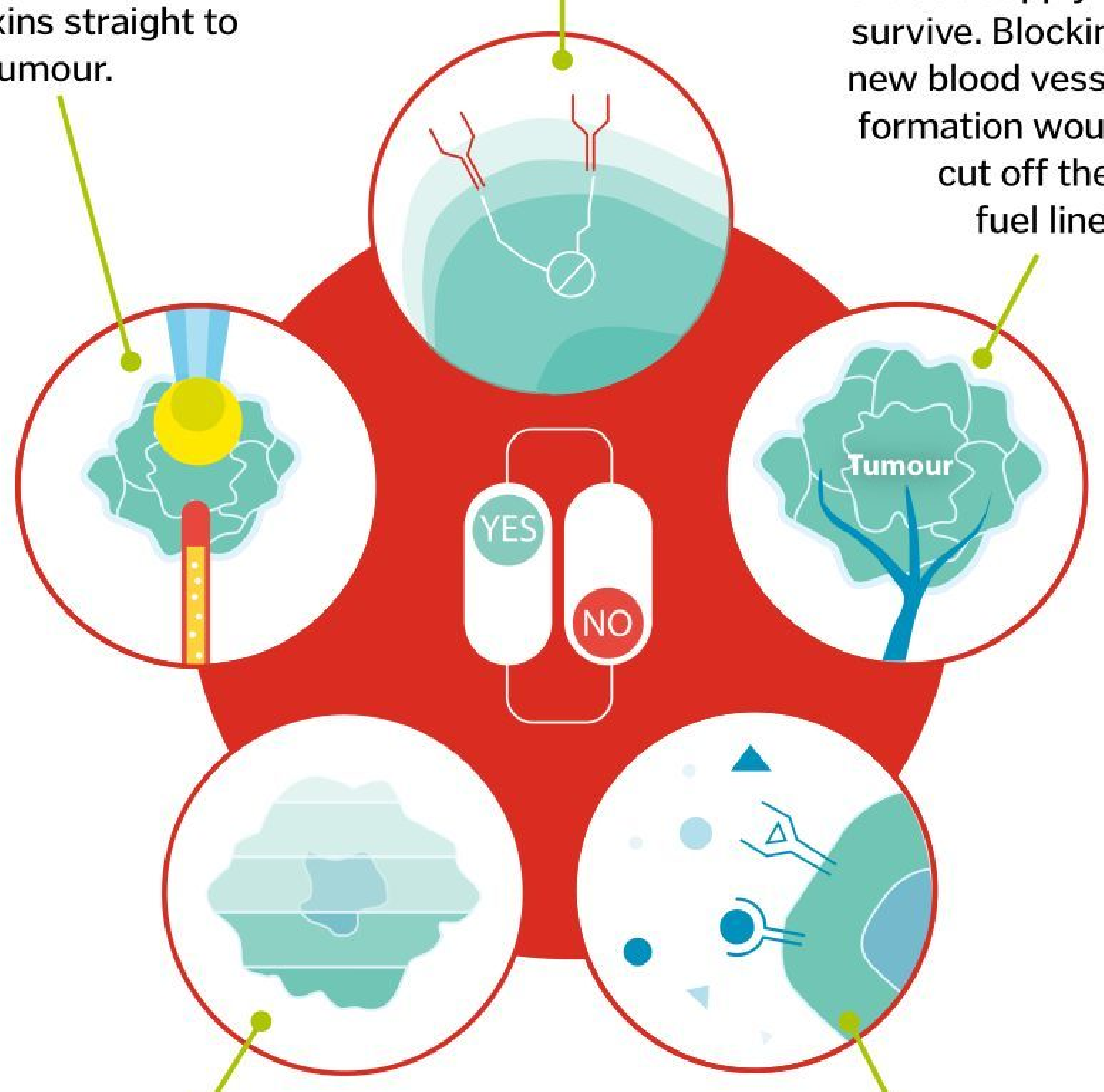
TARGETING CANCER'S WEAKNESSES

MODERN TECHNIQUES ARE ZEROING IN ON THE MOLECULES AND GENETICS THAT MAKE CANCER CELLS VULNERABLE

GROWTH SIGNALS
Cancer cells receive signals that tell them to keep growing. Blocking these could halt the process.

MOLECULAR TAGS
Cancer cell molecules look different. Targeting these could deliver toxins straight to a tumour.

BLOOD SUPPLY
Cancer cells need a blood supply to survive. Blocking new blood vessel formation would cut off their fuel lines.



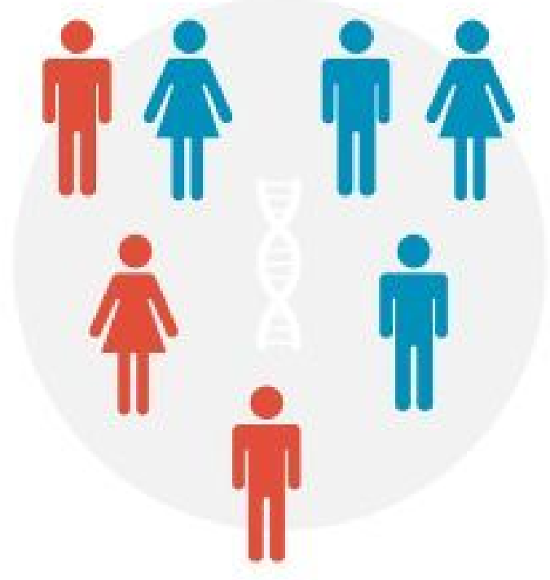
SELF-DESTRUCTION
Cancer cells don't die even though they are faulty. Targeted therapies could switch self-destruct systems on.

HORMONES
Some cancer cells are driven by hormones. Stopping their production could slow growth.

TRAWLING CANCER GENETICS
Cancers have distinctive mistakes in their genetic code that could reveal weaknesses.

PATHOLOGY
Cancer cells can be tested for the presence of molecules that single them out as defective.

CUSTOM TREATMENT
Individual patients could be matched to the treatments most likely to work for their unique tumour.



CUSTOMISING CANCER TREATMENT

The Human Genome Project unravelled the human genetic code in 2003. This epic sequencing mission detailed every single letter of our DNA, revealing for the first time the complete recipe book for a human body. Cancer cells read from the same recipe book as healthy cells, just with words blotted out, pages stuck together and sentences scrambled. By understanding how the recipe book is supposed to be put together, scientists are now better able to identify why and how cancer cells have got it so badly wrong.

Every person is slightly different and their cancer cells start with a slightly different set of instructions, and as the disease progresses, different tumours adapt in different ways. Two women might both have breast cancer, but although there are patterns of similarity, the genetics inside their cancer cells won't be exactly the same, so they don't always respond in the same way to treatment. In the future, people will be tested to reveal the targeted treatments that will work best for them.

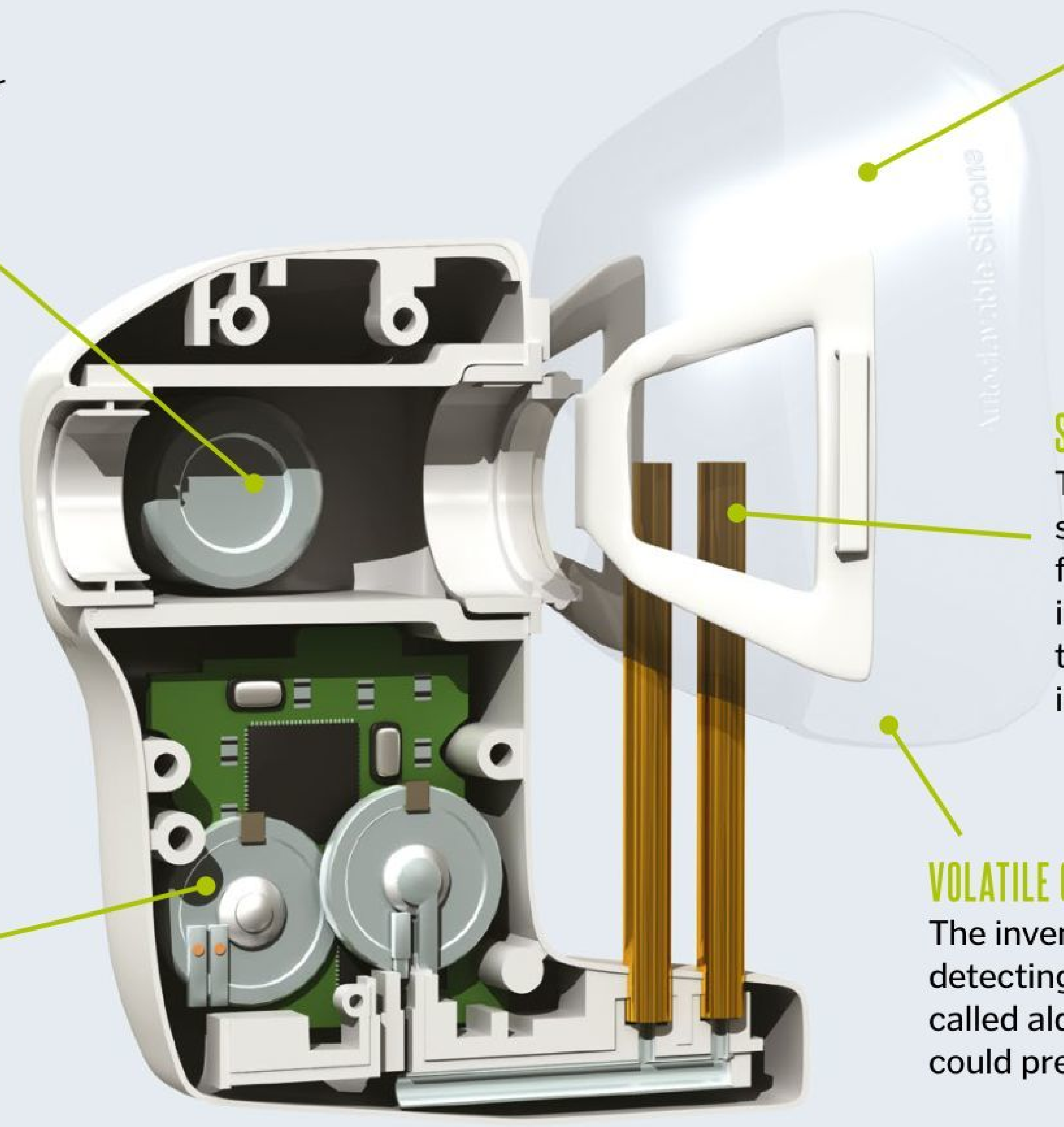
○ Different cancers carry different mistakes and respond differently to treatment

CATCHING CANCER EARLY

The sooner cancer is detected, the easier it is to treat. There are already three screening programmes in operation in the UK to detect bowel cancer, breast cancer and cervical cancer, but in the future things could become a whole lot simpler. Research into 'biomarkers' is searching for molecular signals that could reveal cancer in a simple blood, urine or even breath test.

Biomarkers are molecular signatures unique to different types of cells. Cancer cells differ from normal cells in ways that can already be detected using biopsies of tumour tissue, but researchers think that these differences might also make their way into body fluids, allowing them to be picked up with a simple test. Biomarkers might be able to reveal clues about the best treatment to use, whether the tumour is becoming resistant to current drugs and whether cancer has returned.

> *"One tactic is to cut cancer's fuel lines"*



SENSORS
Sensors detect carbon dioxide and pressure for breath monitoring.

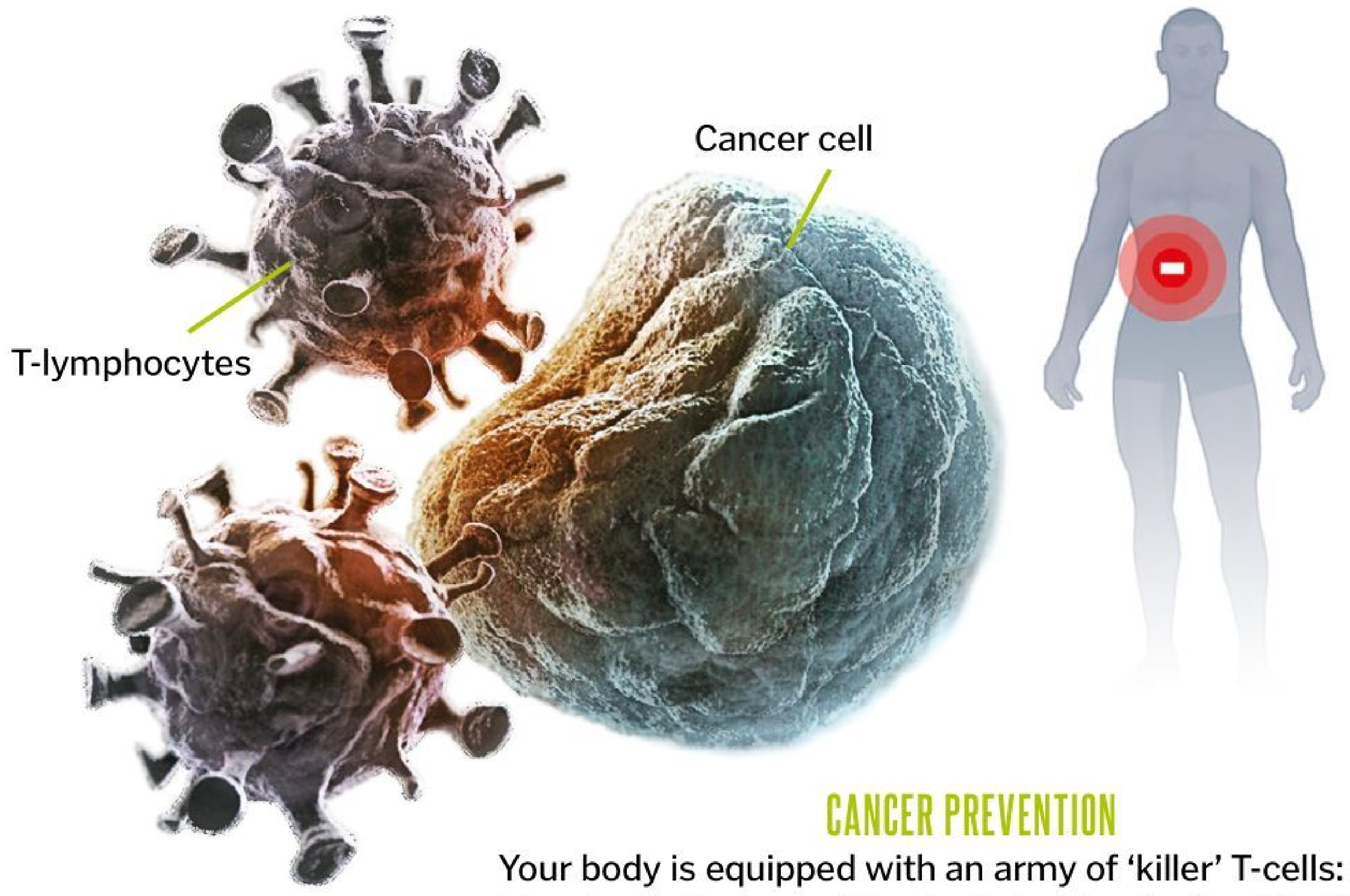
FACEMASK
Single-use masks with a filter are used to blow air into the device.

SORBENT TUBES
The breath is separated into fractions and stored in two pairs of tubes that can be analysed in the lab.

LUCID CLINICAL TRIAL
The device is currently being trialled to find out whether it is effective for lung cancer diagnosis.

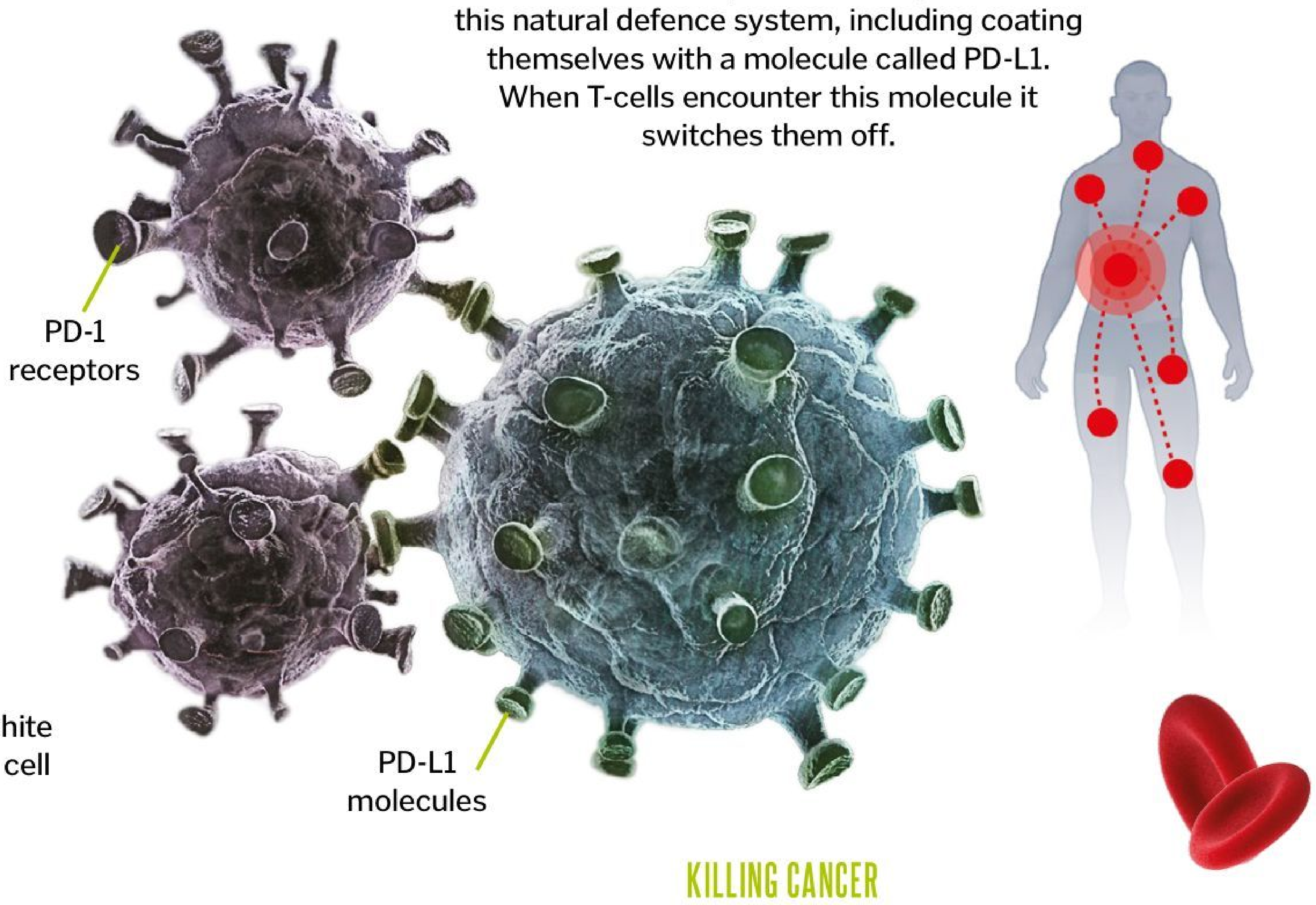
VOLATILE ORGANIC COMPOUNDS
The inventors hope that detecting traces of chemicals called aldehydes and ketones could predict lung cancer.

STRENGTHENING YOUR IMMUNE ARMY



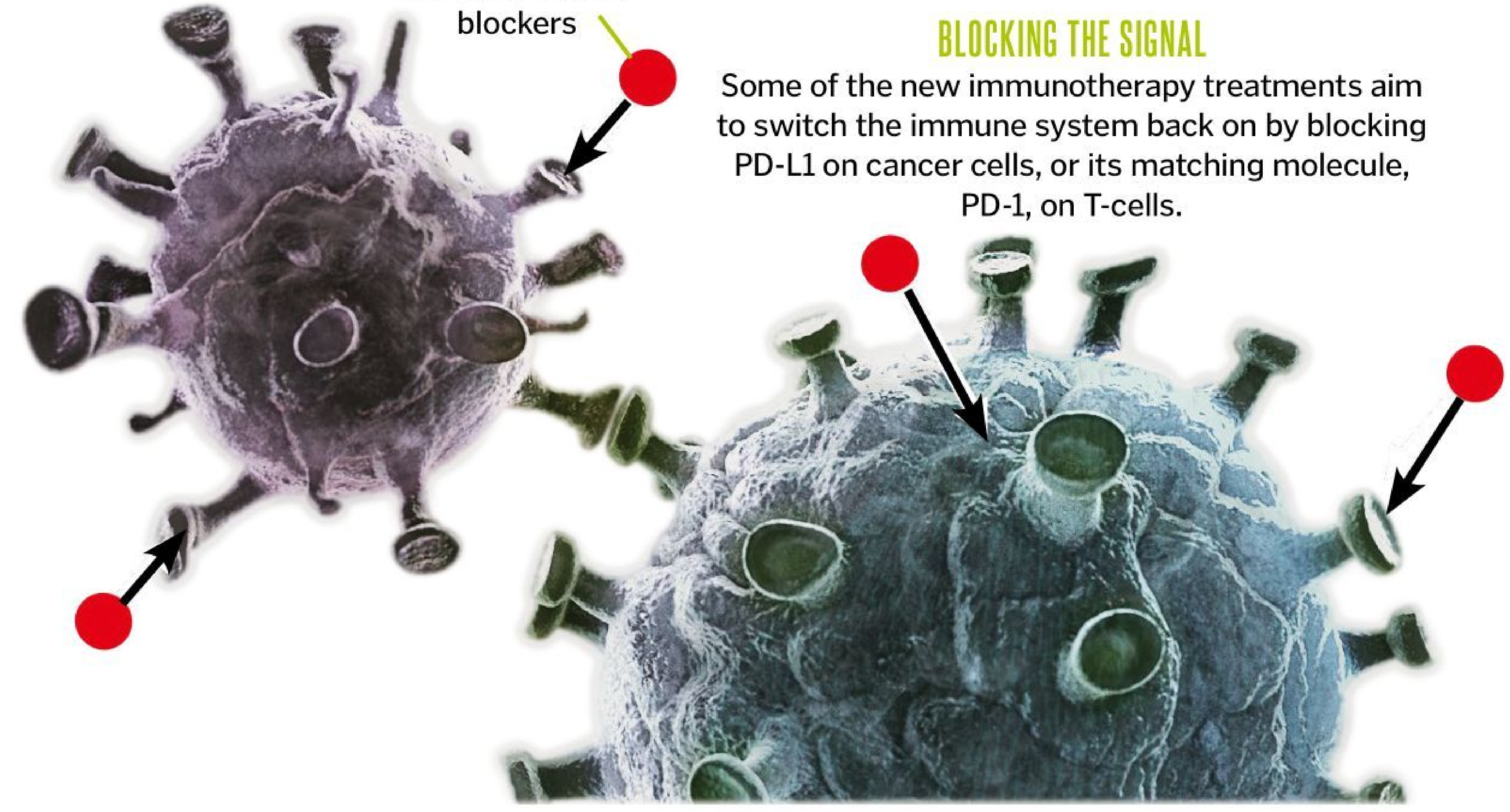
CANCER PREVENTION

Your body is equipped with an army of 'killer' T-cells: white blood cells that patrol the body looking for trouble. If a cell starts to go wrong, these cells come in and kill it.



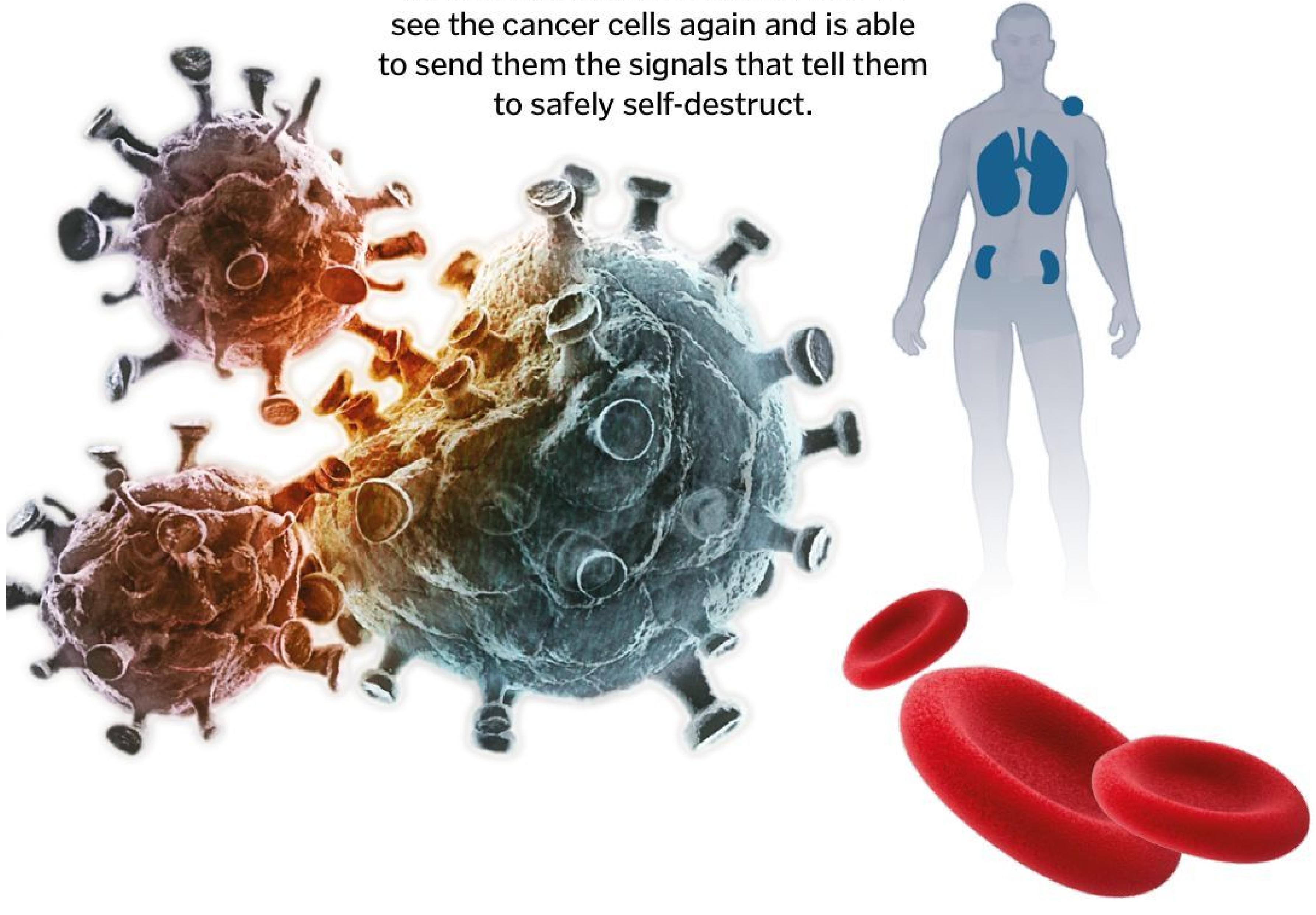
SUBTERFUGE

Cancer cells develop different ways to evade this natural defence system, including coating themselves with a molecule called PD-L1. When T-cells encounter this molecule it switches them off.



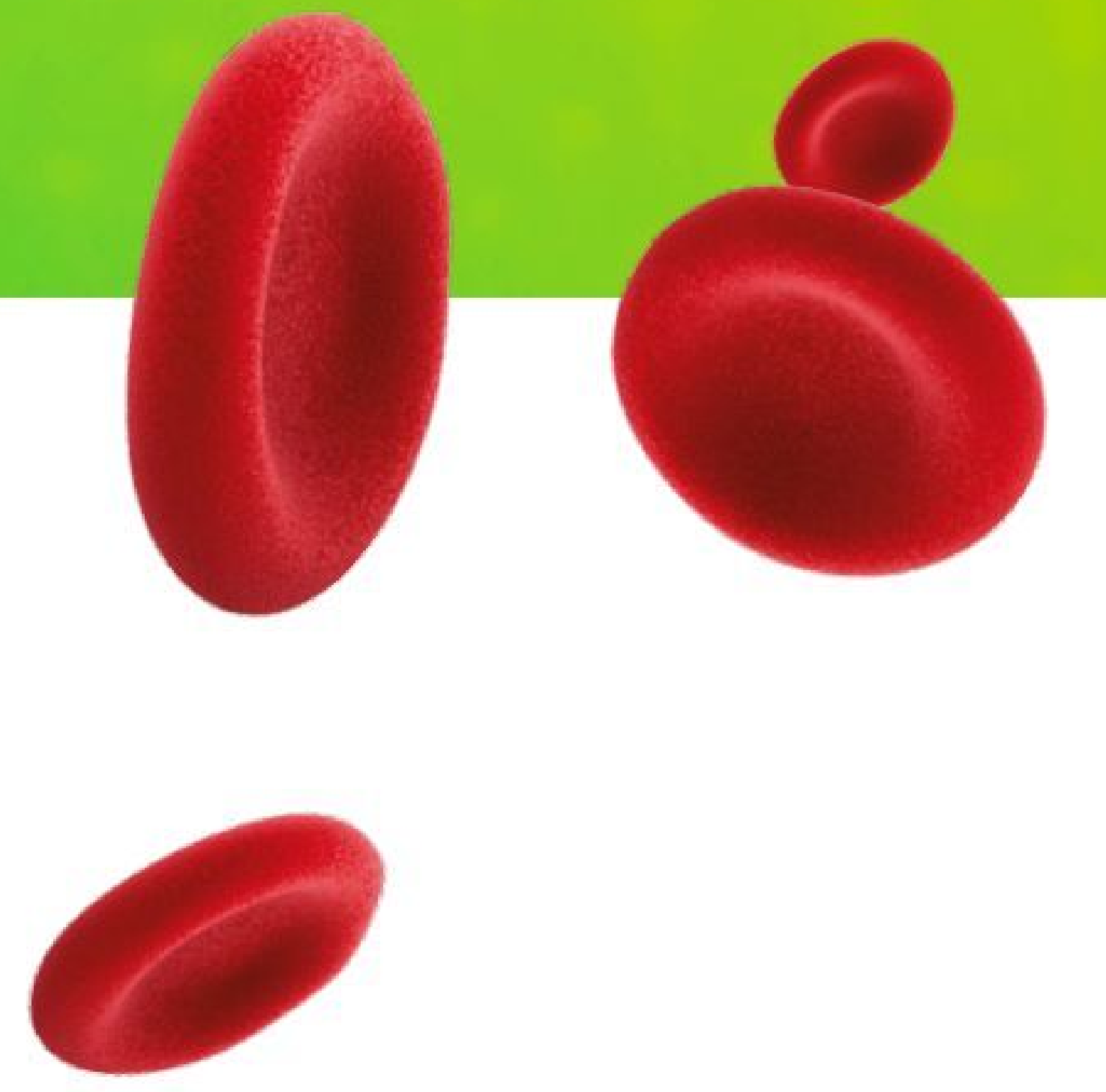
BLOCKING THE SIGNAL

Some of the new immunotherapy treatments aim to switch the immune system back on by blocking PD-L1 on cancer cells, or its matching molecule, PD-1, on T-cells.



KILLING CANCER

The immune system is then able to see the cancer cells again and is able to send them the signals that tell them to safely self-destruct.



EXPERT OPINION

HOW IT WORKS SPOKE TO AN IMMUNOLOGIST AND A RESEARCH NURSE ABOUT THE FUTURE OF CANCER TREATMENT

THE IMMUNOLOGIST

Dr Edd James *is an associate professor in cancer immunology at the University of Southampton, one of the country's leading centres for immunotherapy research*

Could you tell us a bit about your research? What are you trying to find out?
The immune system, in particular the 'infantry' known as killer T-cells, are able to detect cancer cells through examining small protein fragments presented on larger proteins called MHC at the surface of cells. Almost all cells have these MHC molecules and they act as a way to understand what is going on in the cell at that moment. Despite these molecules, cancer cells are able to 'hide in plain sight' from the killer T-cells. We are investigating how they do this and how to either reverse this process or re-educate the killer T-cells to be able to 'see' the cancer cells through changing what the MHC molecules show them.

Why can't the immune system just kill cancer cells on its own?
In many instances, the immune system does kill cancer cells at an early stage of development without us knowing about it. However, cancer cells 'evolve' to hide themselves to prevent the immune system from finding and attacking them. In addition, the cancer cells are able to promote an environment that suppresses the immune response, thus preventing it from working properly.

How does immunotherapy help?
Immunotherapy works in many ways, but there are two main methods by which it can help. The first is to target molecules that the cancer cells have on the cell surface using proteins called antibodies. These are specific for particular molecules and once bound to the target molecules serve to highlight the targeted cancer cells to the immune system. This allows them to be identified, attacked and destroyed.

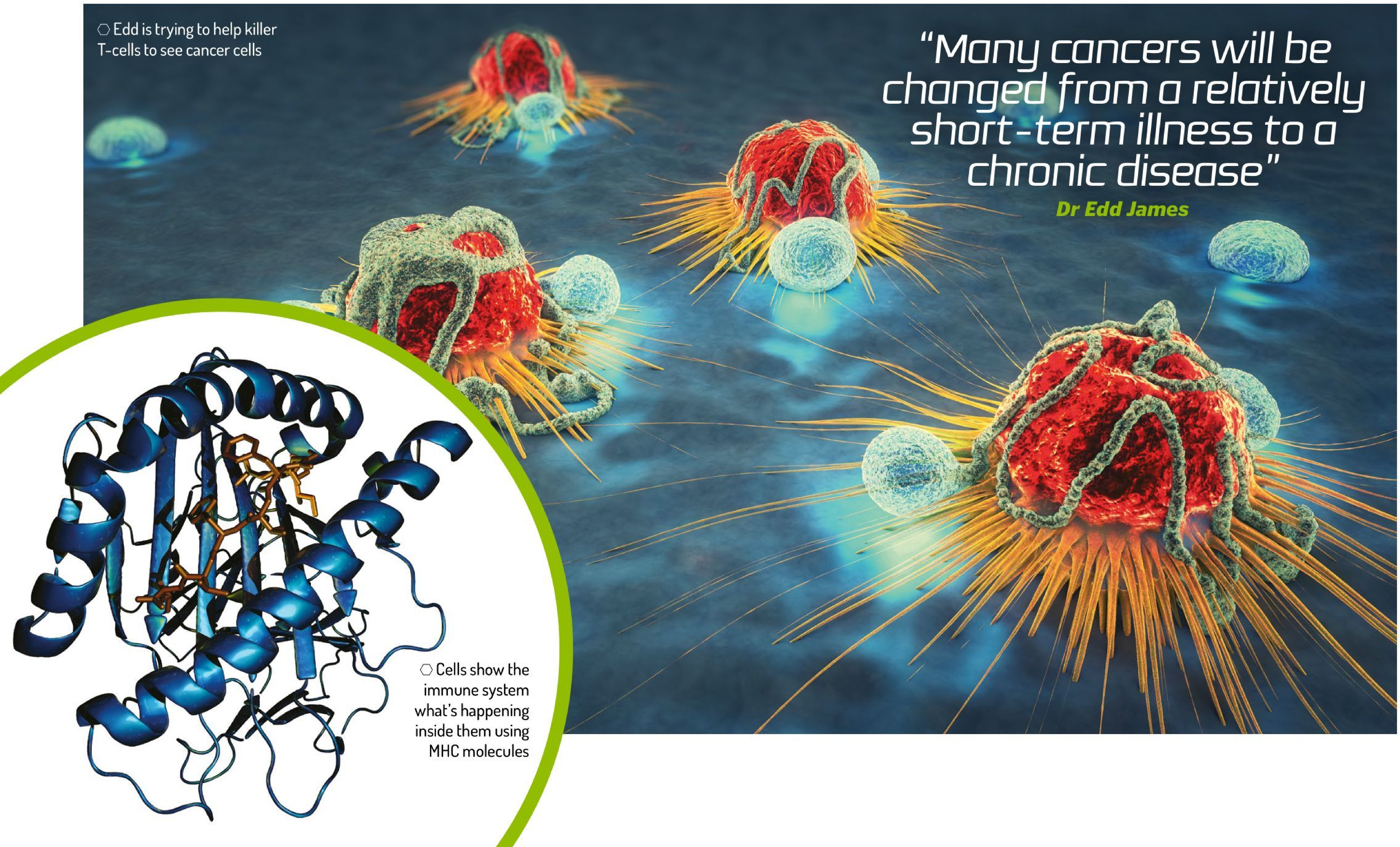
The second method is to target the killer T-cells themselves. Cancer cells are able to put the brakes on the killer T-cells to prevent them working properly. This occurs because the cancer cells deliver a negative, inhibitory signal to the killer T-cells through interaction. These signals are produced through a number of different molecules that can be blocked using antibodies. Blocking these interactions prevents the negative signals and allows the killer T-cells to work normally and kill the cancer cells.

What needs to be done next to make immunotherapy better?
Currently the therapies that are used are relatively blunt tools and aren't effective in many people. We need to understand how the cancer blocks the immune system in greater detail. This will give us a better appreciation of the processes involved in allowing cancer cells to evade the immune system and also allow us to identify new molecules to target.

There are many new investigations looking to combine current immunotherapies to improve their success. In trials these are working much better. However, a major downside of many of these combinations is an increase in side- effects that needs to be addressed.

Do you think we will ever cure cancer?
There is likely to be an effective cure for a number of cancers in the future. Our greater understanding of the molecular aspects of a cancer, and how to utilise the immune system more effectively to kill the cancer, will greatly increase possible treatments and improve their efficacy. This will allow a much more personalised approach to treatment based on the molecular characteristics of the cancer.

These advances will mean that many cancers will be changed from a relatively short-term illness to a chronic disease, where patients are treated as and when cancer arises. This will increase cancer-free survival, effectively enabling many people to live a normal lifespan.



Edd is trying to help killer T-cells to see cancer cells

> "Many cancers will be changed from a relatively short-term illness to a chronic disease"
> **Dr Edd James**

Cells show the immune system what's happening inside them using MHC molecules

THE RESEARCH NURSE

***Jac Samuel** is a CRUK senior research nurse. She leads a team of research nurses delivering clinical trials testing brand-new cancer treatments for the first time*

Could you explain a bit about what research nursing is?
Research nursing is a really interesting career pathway, which most nurses when they qualify don't even consider. You think you're going to work on a ward, and you obviously go into nursing because you want to look after people and help them. Research nursing is interesting because you're working with new treatments that are not licensed.

It's a process of gathering data, which is then analysed to see whether or not this new treatment is comparably better than what we've currently got. It might be that it works better, or it might be that it doesn't work any better but it doesn't have such bad side-effects. Or maybe, instead of giving it via somebody's vein, they might be able to take it in the form of a tablet.

As a research nurse you're delivering those treatments to patients. We don't know how well it works, so we're conducting an investigation. What we're aiming for is really good quality data that can be analysed to prove how well something is working.

Why do treatments have to go through trials?
You can't just give something from a lab because you don't know how it works. Even if it's worked in an animal model, you don't know how it's going to work in a human. Everything has to be tested to make sure it's safe. Otherwise you could have some company saying, 'Hey, we think this really works and it's a cure, and we're going to charge you £50,000 for it' but there would be no evidence for that.

The whole point of research is that it's evidence-based. The laboratories will create the treatment, and they will test it in a cell line and in an animal model, but it's very different to how it might work in a human.

What changes have you seen in cancer treatment?
I've been nursing for a long time now, but even in the last five years actually it has really changed. Scientists have so much more understanding now of the intricacies of cells. Before, there used to be a blanket term for several different sorts of cancer. It's so much more nuanced now, and I think this is only the tip of the iceberg.

There have been certain drugs that have turned it around for patients. Five or ten years ago, you knew with their diagnosis that their prognosis was not great, and yet now you're seeing patients with exactly the same type of disease out of treatment and going strong.

Do you think that there will ever be a cure for cancer?
I think it's really difficult to say that there is going to be one single cure for cancer. The trouble is cancer is such an umbrella term. You've got so many different sorts of cells in your body, and cancer can affect different types of cells in different ways.

I think that as we've seen such a big change in survival rates in the last ten or 15 years, in the next ten or 15 years you're going to see big breakthroughs that are going to make huge differences. We still don't have a cure for cancer, but more people are surviving cancer and their quality of life is better with their treatment, and I think that will continue.

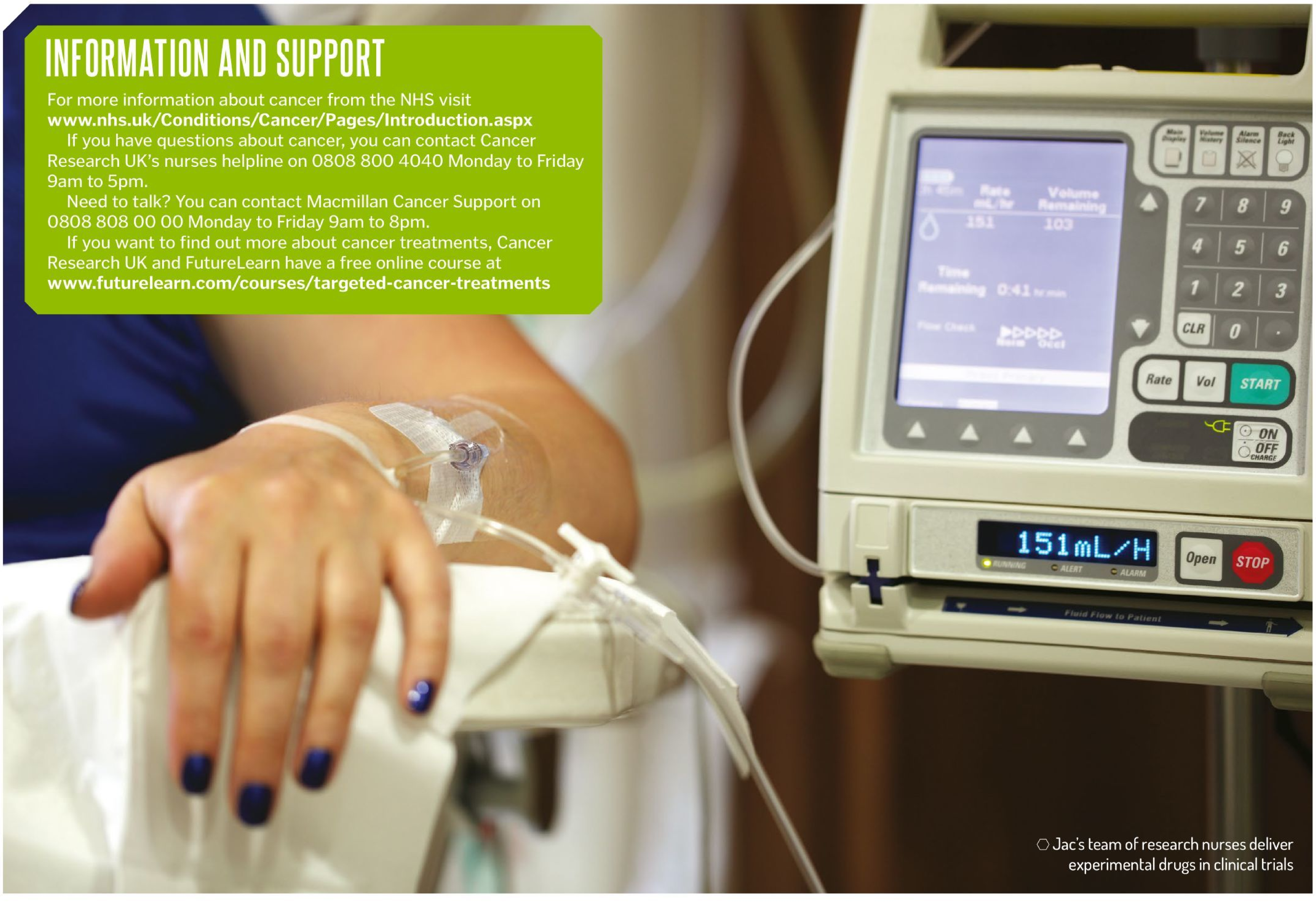
INFORMATION AND SUPPORT

For more information about cancer from the NHS visit **www.nhs.uk/Conditions/Cancer/Pages/Introduction.aspx**

If you have questions about cancer, you can contact Cancer Research UK's nurses helpline on 0808 800 4040 Monday to Friday 9am to 5pm.

Need to talk? You can contact Macmillan Cancer Support on 0808 808 00 00 Monday to Friday 9am to 8pm.

If you want to find out more about cancer treatments, Cancer Research UK and FutureLearn have a free online course at **www.futurelearn.com/courses/targeted-cancer-treatments**



○ Jac's team of research nurses deliver experimental drugs in clinical trials

THE FUTURE OF MEDICINE

HOW ARE WE GOING TO BEAT THE WORLD'S DEADLIEST DISEASES?

Medical science has produced some incredible solutions to challenging problems over the decades, from antibiotics to fight bacterial infection to imaging technologies to look inside patients without using a knife. It's hard to predict what will happen next, but science has recently opened some really exciting doors to the future of medical treatment.

Medicine is no longer just about biology and drugs. Computing, engineering, nanotechnology and many more disciplines are now providing new solutions to age-old problems.

In the hospitals of the future augmented reality could allow surgeons to see through their patients, and contact lenses could monitor blood sugar for diabetics. Prosthetic limbs linked directly to the nervous system could allow amputees to move and feel just by thinking, while 3D printers could be utilised to create custom medical kit, or even fully working replacement organs, on demand.

We are learning how to retrain our own immune systems to fend off deadly diseases, and we are developing technology that could allow our own genetics to be tweaked and changed on the go. The scientific community has access to a massive and rapidly expanding pool of data from patients the world over, and as we dig deeper into the biochemistry of illness, new ways to precisely treat disease are set to appear.

One day wearable tech and at-home test kits could monitor for the first signs of sickness, and custom treatments might be delivered based on our own unique genetic and biochemical fingerprints, minimising side-effects and maximising our chances of recovery.

HOW GERMS SPREAD

WARNING DO NOT FILL ABOVE THE LINE
DANGER
DESTROY BY INCINERATION

BODY FLUIDS

Blood, saliva, semen and breast milk can all carry disease

Liquids provide an excellent way for pathogens to travel around. Precautions are always taken when dealing with bodily fluids in hospitals and labs because contaminated fluids can transmit diseases such as mumps and HIV.

FOOD AND DRINK

Contaminated food and drink carry pathogens into the gut

Stomach acid provides some protection, but it can't stop everything. Pathogens enter through the mouth and set up home in the digestive tract or move into the body through its walls.

SKIN TO SKIN CONTACT

Infections can be spread by contact

Chickenpox, cold sores, head lice and warts can all be transmitted by touching someone with the infection; the viruses, bacteria or parasites simply move from one person to another. Some of these examples can also survive on inanimate surfaces for a short time.

DROPLETS

Pathogens can be transmitted short distances by drops of liquid in the air

Tiny drops of fluid released by a cough or a sneeze travel around a metre before they settle onto door handles, surfaces and skin. It's an easy way for respiratory infections to spread.

PREVENTING HISTORY'S BIGGEST KILLERS

VACCINATIONS TEACH THE IMMUNE SYSTEM HOW TO FIGHT BEFORE IT ENCOUNTERS THE REAL DISEASE

Our natural defence against disease is our immune system. This army of cells work together to patrol the body and destroy anything that shouldn't be there. It's split into two parts: a fast-response 'innate' system that wages war at the first sign of trouble and a slow, specialised 'adaptive' system that delivers a stronger and more focused attack.

The first time the immune system meets a new infection it takes up to a week for the specialised immune cells to appear. In this time the pathogen can multiply and people can become very sick. Vaccinations bypass this step by giving the immune system an opportunity to train beforehand.

The first vaccine was developed by Edward Jenner in 1796. He noticed that milkmaids didn't catch smallpox; they were exposed to a similar disease, cowpox, and their immune systems were better trained. Jenner tried infecting children with cowpox and found that they too gained protection against smallpox.

Vaccinations have been developed against dozens of infectious diseases since, and they are now being made to teach the immune system to fight other illnesses, too.

TRAINING THE IMMUNE SYSTEM

Vaccinations are like a training programme for your immune system, giving it a sneak peek at enemies that it might encounter in the future so that it can prepare in advance. They can be made in different ways but usually contain inactive bacteria or viruses, or examples of molecules that the pathogens make.

When the vaccination has been injected your immune system comes to have a look. It will examine the parts of the pathogen and work out the best way to attack, as though it were fighting the real thing. After the vaccine has been cleared up some of the cells that fought it remain in the body on patrol as 'memory cells'.

When you encounter the real pathogen, your immune system will be ready to respond. Instead of spending time working out what to do, the memory cells left over from the vaccine instantly clone themselves, producing an army of cells that can clear the infection before you get sick.

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THE END OF HIV

HOW DO YOU HUNT DOWN A VIRUS THAT'S HIDING IN YOUR OWN IMMUNE SYSTEM?

Human Immunodeficiency Virus (HIV) hijacks the immune system. The virus gets inside, inserts its genetic code into the genome of a cell and transforms it into a factory to make more of the virus. While this is happening the cell is unable to function normally and gradually, as more and more cells are taken over, the immune system is left seriously weakened. The result is known as Acquired Immune Deficiency Syndrome (AIDS).

HIV is now treatable with a combination therapy that stops the virus from replicating. The amount of virus often dips so low in the blood that the disease can't be passed on. Transmission from mother to child is also being eliminated with new drugs. However, not everyone has access to treatment.

The gold standard for the future of HIV medicine would be a vaccine that can teach the immune system to neutralise the virus with a coating of antibodies. In theory, this could be used not only to prevent infection but also to stop the disease coming back in people who have some of the virus still hiding in their systems.

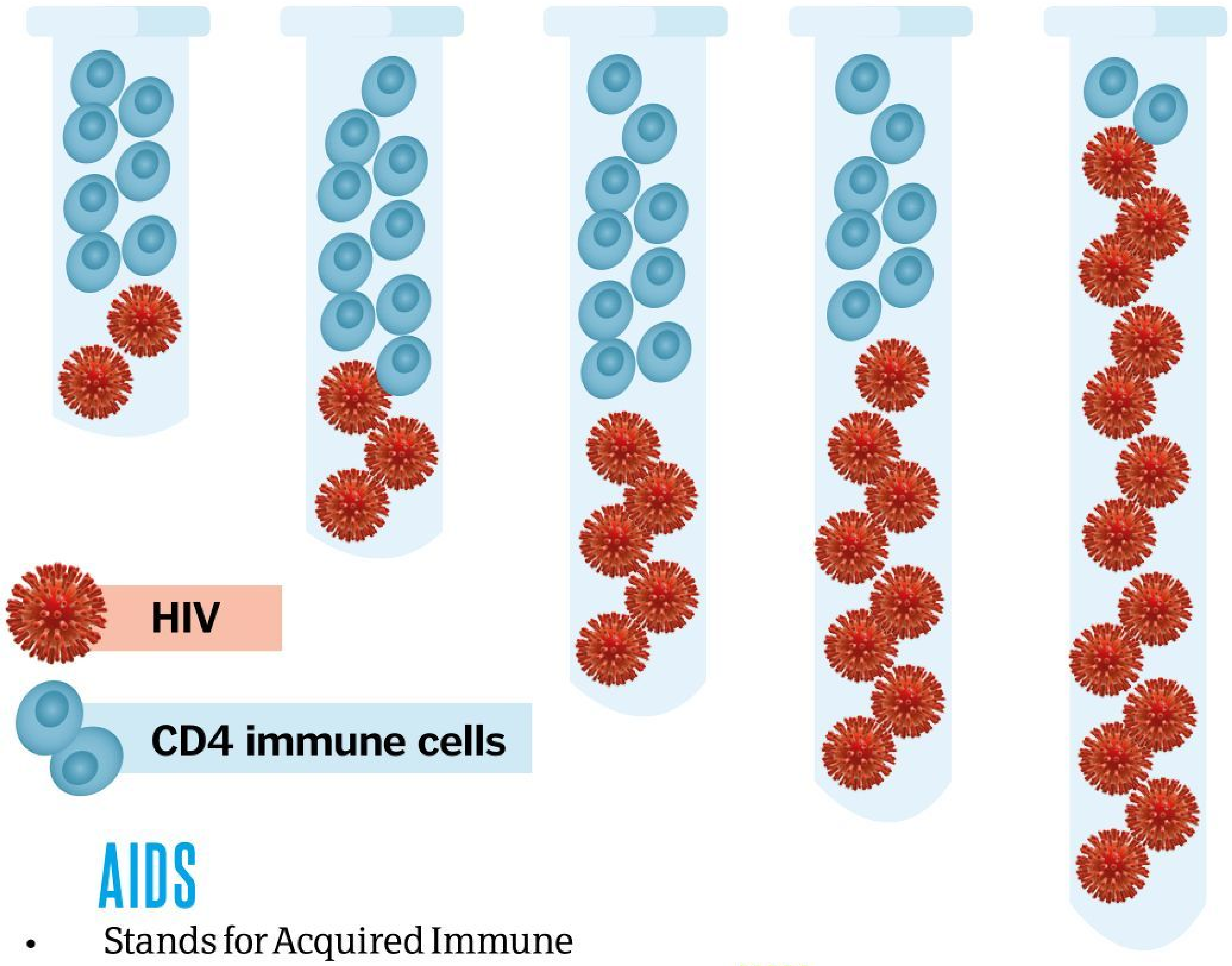
This is a huge challenge; the virus shape-shifts to avoid detection and the immune system doesn't usually respond. But new vaccines are being trialled all the time, and as our understanding of HIV and the immune system improves, we are inching closer to making it a reality.

HOW HARD IS IT TO CURE?

HIV stitches its own genome into the genome of a particular type of immune cell (white blood cells known as CD4) so that the two are permanently linked together. Antiretroviral treatment can stop the virus from making copies of itself, but they can't get rid of it completely unless the immune cells themselves are killed.

This has only ever been done once, in 2007. The Berlin Patient had cancer and needed a bone marrow transplant. His own immune system, carrying HIV, was destroyed and replaced with donor cells. They had a genetic mutation that made it harder for HIV to infect them, and the patient was cured of the virus.

Bone marrow transplants are risky, however, and there aren't enough donors available, so it's not a practical solution to rid the world of HIV altogether.



AIDS

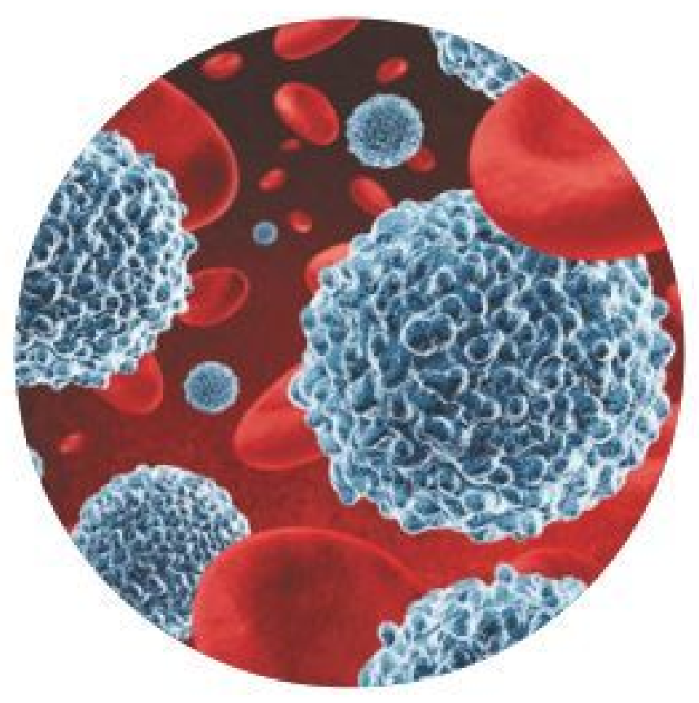
- Stands for Acquired Immune Deficiency Syndrome.
- Is the disease caused by HIV.
- Takes advantage of the damaged immune system that is unable to fight it.
- People die due to infection or resulting cancer.

HIV

- Stands for Human Immunodeficiency Virus.
- Is the virus that causes AIDS.
- Infects the immune system.
- Infection compromises the cells of the immune system.

TIMELINE

1981
Men in California start to fall ill with unusual infections after their immune systems become weakened.



1983
Scientists discover that Human Immunodeficiency Virus (HIV) is the cause of Acquired Immune Deficiency Syndrome (AIDS).

1985
Commercial blood tests for HIV are invented, allowing screening to begin.

1987
The first drug treatment for HIV, azidothymidine, is approved.

1996
Triple-drug therapy is introduced, turning HIV infection into a long-term disease.

2007
A single patient in Berlin is cured by a pioneering bone marrow transplant.

FUTURE
A vaccine is developed to train the immune system to attack HIV.

FUTURE
A drug is developed to reveal HIV lurking in dormant cells.

37 million

In 2015, nearly 37 million people were living with HIV

Over half of people with HIV can't access treatment

1.1 million

people die as a result of AIDS each year

HIV is transmitted through body fluids, including blood, semen and breast milk

8 out of **10** pregnant women with HIV receive treatment to minimise the risk to their child

HIV infects the immune system, crippling the body's defences

40%

of people with HIV don't know they're infected

Antiretroviral therapy stops the virus replicating

Condoms, HIV testing and circumcision help to reduce transmission

HIV puts people at risk of catching other diseases like tuberculosis

CAN CANCER BE CURED?

HUGE PROGRESS HAS BEEN MADE OVER THE PAST CENTURY, BUT WHAT HAPPENS NEXT?

Cancer is an ancient disease; tumours have been found in Egyptian mummies and even in the fossils of dinosaurs. It happens when genes involved in growth and repair go wrong. Affected cells make copy upon copy of themselves, and these new cells start to break away, travelling around the body and making yet more copies elsewhere.

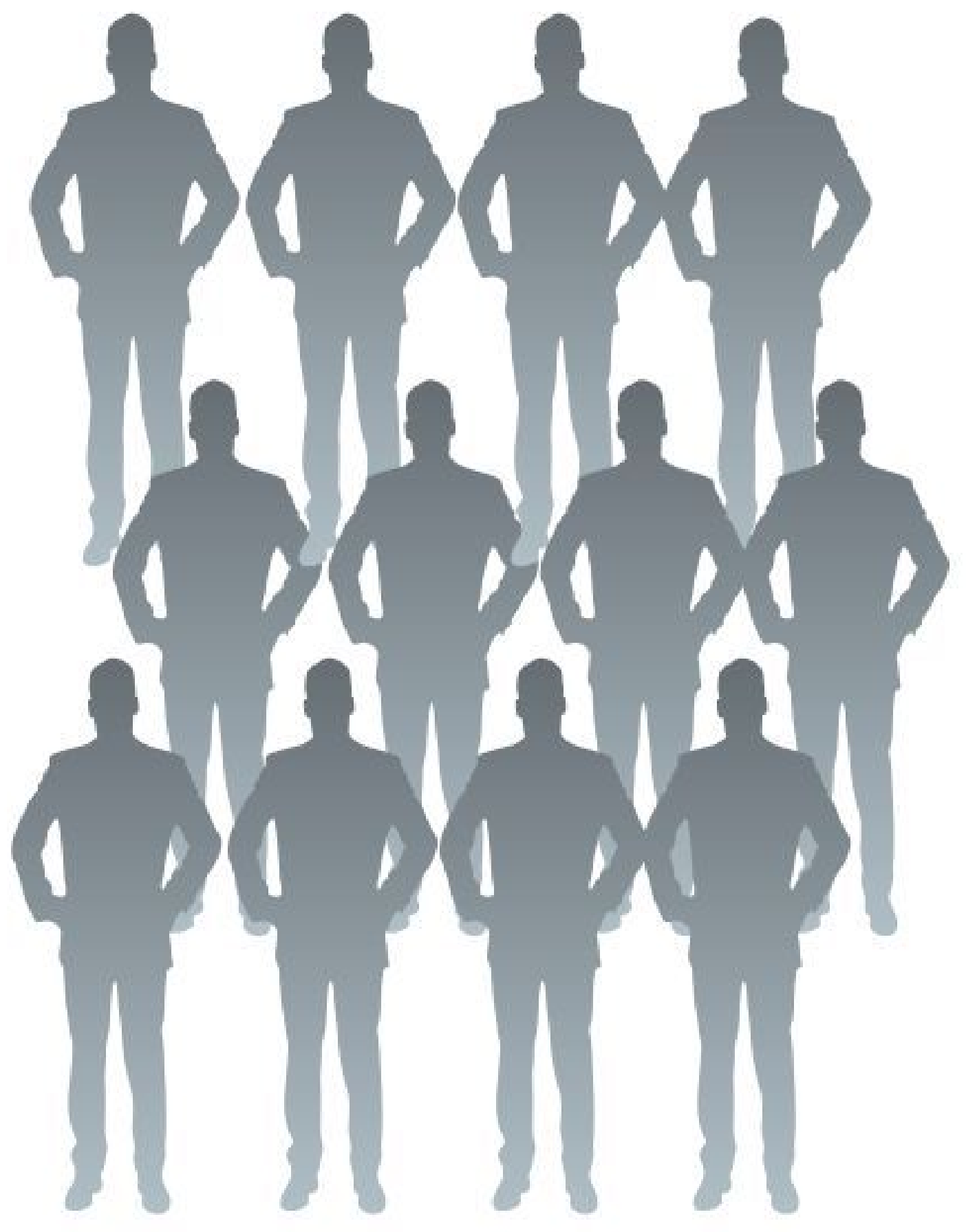
If cancer is caught early, it can already be cured. If the tumour is removed, the cancer is gone. However, once the cancer has spread it is harder to treat, and the more it spreads, the less likely people are to survive.

Stopping cancer before it really starts would be the best option. Vaccinations might be used to train the immune system to recognise cancer cells, or a routine blood or breath test could be developed to pick up the earliest signs of the disease. However, the likelihood of cancer increases with age, and with people living longer, the incidences are rising.

For those who do develop the disease, several futuristic treatment options are already being developed. Future humans could end up having their immune systems retrained and augmented, or they might receive genetically engineered viruses designed specifically to infect and kill the tumour. We might even be able to switch genes on and off inside tumour cells to halt their growth.

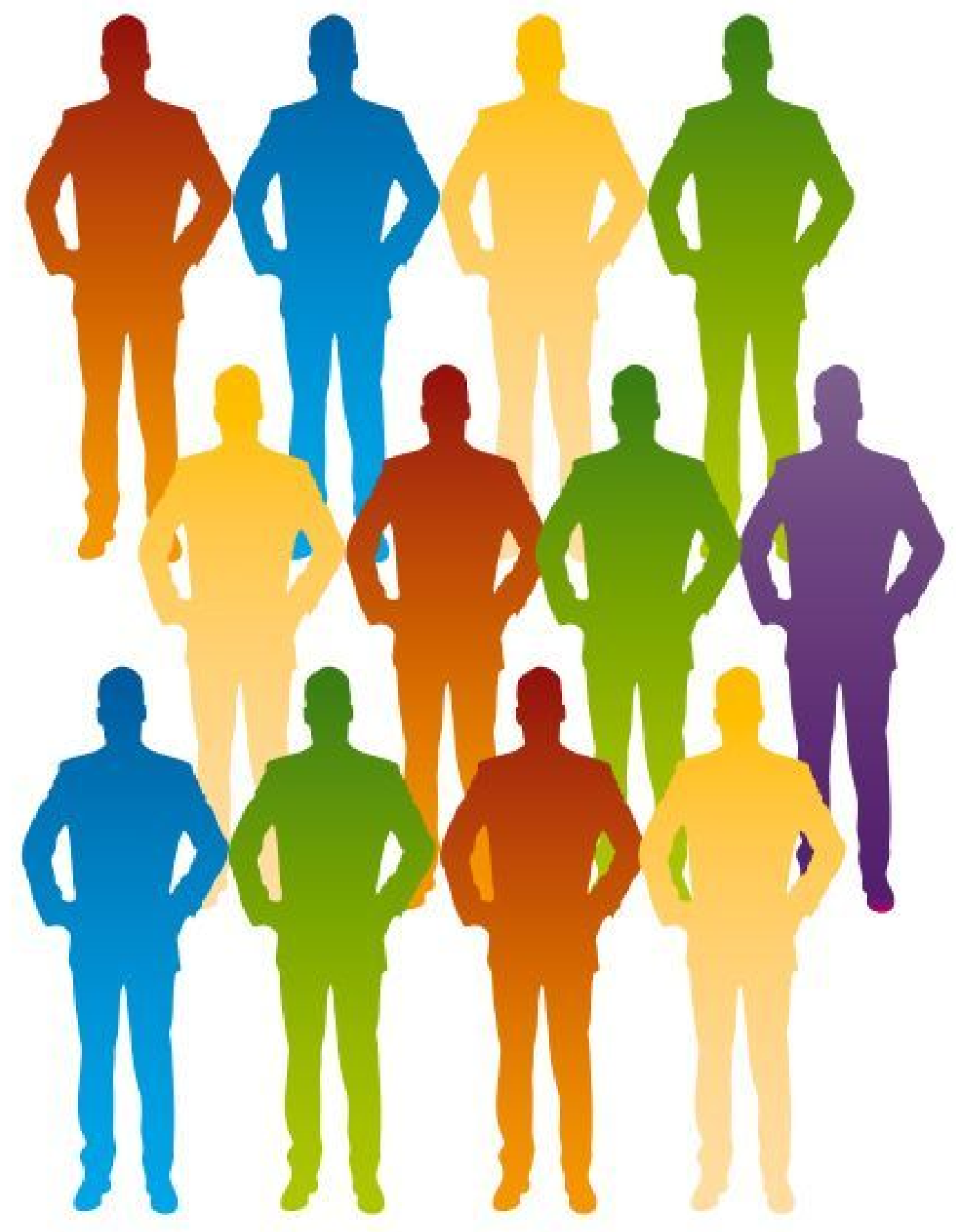
THE FUTURE OF CANCER MEDICINE

MATCHING PEOPLE TO THE RIGHT TREATMENT COULD BE THE ANSWER TO CONTROLLING CANCER



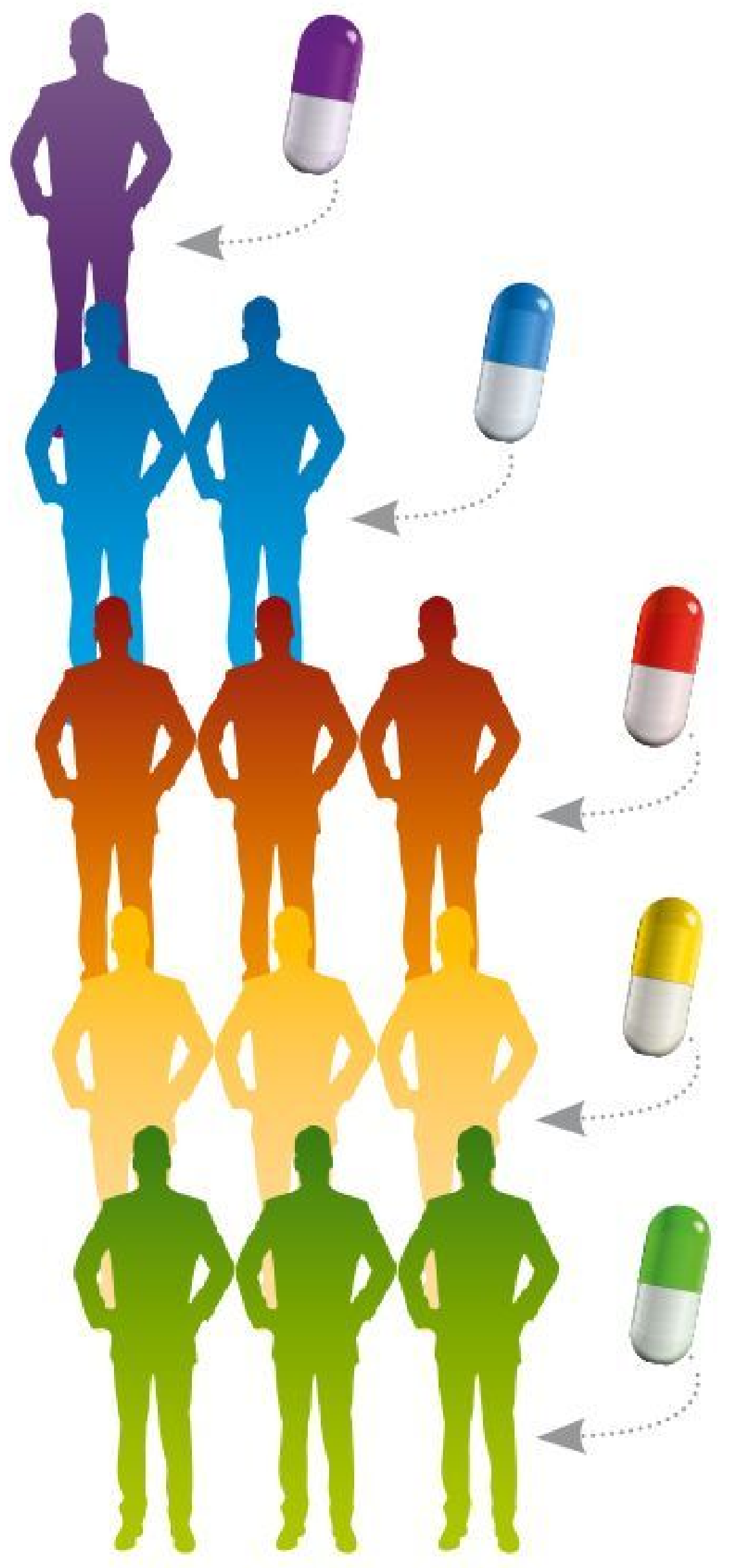
GROUP OF PATIENTS

Several people might have brain cancer, but not all brain cancers are the same.



GENETIC TESTING

The patients are tested to find out the exact genetic and chemical makeup of their tumour.



TREATMENT MATCHING

Patients are matched with treatments that specifically target the weaknesses of their own cancer.

WHERE IS THE CANCER CURE?

Cancer gets a lot of research money, and thousands upon thousands of scientists are working to try and find the cure, so where is it? If you can cut the tumour out before it has a chance to spread, you can cure it, but if any cells have escaped they need to be found. Radiotherapy and chemotherapy can help to mop up stragglers, but they don't always work, and some cancer cells develop ways to avoid them. The big challenge is that everyone is different, and so too are everyone's cancers. Tumours don't just differ between people, they also change over time. The challenge is to find out how they change and how these different weaknesses can be targeted with treatments.

TIMELINE

1846
The invention of general anaesthetic paves the way for surgery to finally remove tumours.

1880S
The first mastectomy is performed, providing a new treatment option for breast cancer.

1903
Radium is used to treat skin cancer in what is the first example of radiotherapy.

1949
The first chemotherapy drug is approved. It is nitrogen mustard, a WWII weapon.

1950S
Smoking is finally shown to cause lung cancer, encouraging millions to give up.

1990S
Cancer mortality starts to drop in developed countries as diagnoses and treatments improve.

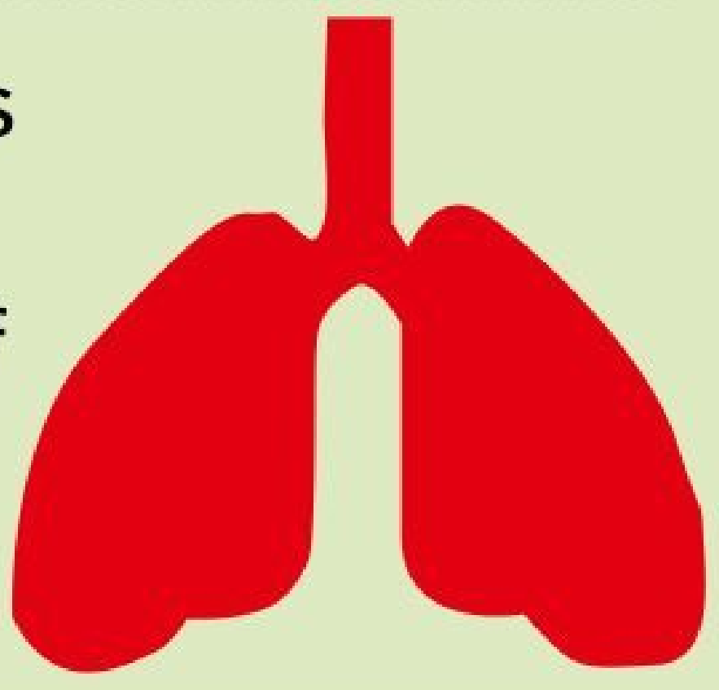
FUTURE
Personalised medicine becomes reality, with patients matched to treatments based on their genes.

FUTURE
A simple blood test is developed to pick up the very earliest signs of cancer.

14 million
people are diagnosed with cancer each year

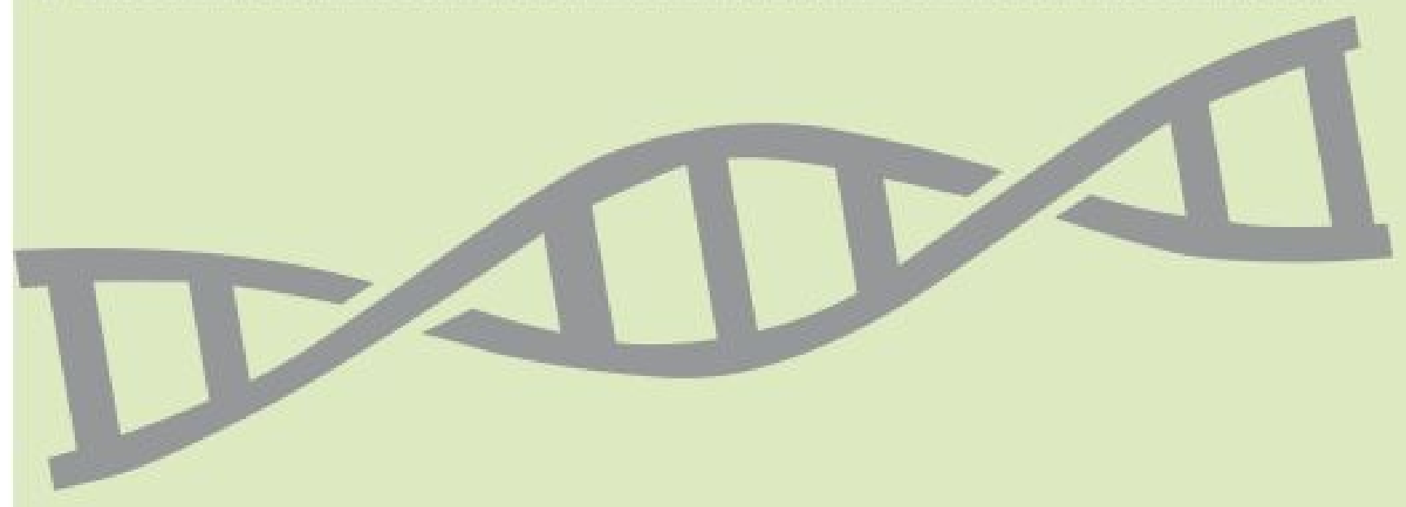
9 million
people die due to cancer each year

Lung cancer is the most deadly type of cancer for both genders



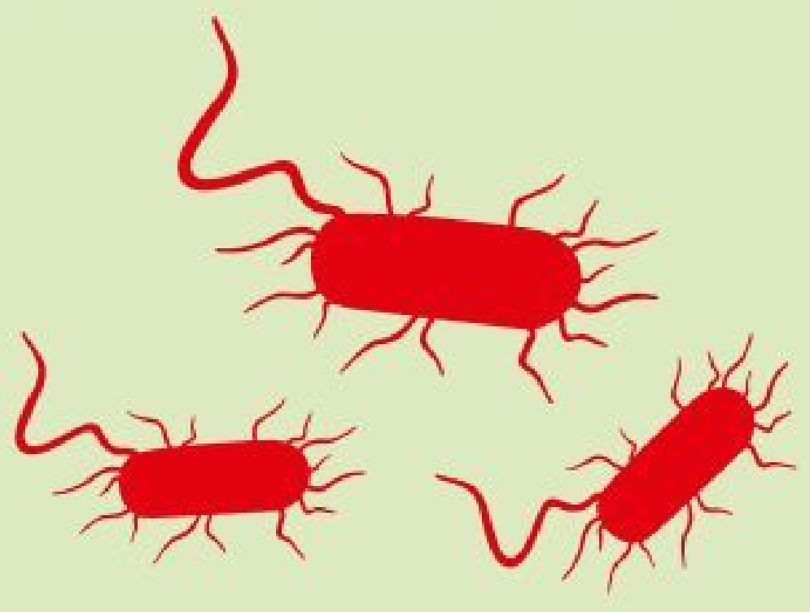
Breast cancer is the most common type of cancer in women

The older you are the more likely you are to get cancer



Cancer is not contagious but it can be genetic

Viral infections can cause some cancers



The earlier cancer is detected, the easier it is to treat

Lifestyle changes could prevent a third of cancers

ELIMINATING MALARIA

THIS DEADLY DISEASE IS CARRIED BY MOSQUITOES, BUT WORK IS BEING DONE AROUND THE WORLD TO WIPE IT OUT

Just one mosquito bite is enough to kill you in some parts of the world. Inside the midgut of Anopheles mosquitoes, gametocytes from the plasmodium parasite mature and combine. These are the equivalent of human sperm and eggs, and the result is hundreds of newly formed parasites ready to infect their next victim.

The parasites migrate up to the mosquito's salivary glands and when it feeds again they enter the human bloodstream. They infect cells in the liver and begin to divide, before spreading back into the blood. As they continue to grow, the cells split open, releasing even more parasites and causing havoc for the body.

Malaria parasites can't reproduce without both mosquitoes and humans, giving us a tantalising opportunity to eliminate them. One idea is to genetically modify colonies of mosquitoes and release them to breed with their wild counterparts; this could be used to introduce damaging genetic traits into the population, either killing the parasites or killing the mosquitoes themselves. Another option is to develop fungi that can infect and kill the insects.

Other options for elimination include designing new insecticides to keep insect numbers down and developing a vaccine to halt transmission.

10-18

Days it takes for malaria parasites to reproduce inside a mosquito

Malaria was first written about in ancient China in 2,700 BCE

3.2 billion

people live in regions where they are at risk of catching malaria

400,000

people die of malaria each year

70%

of malaria deaths are children under the age of five

Malaria is caused by parasites that infect humans and mosquitoes

Spraying houses with insecticide is the best way to stop transmission

Last year **95** countries reported cases of malaria

214 million

cases of malaria were reported in 2015

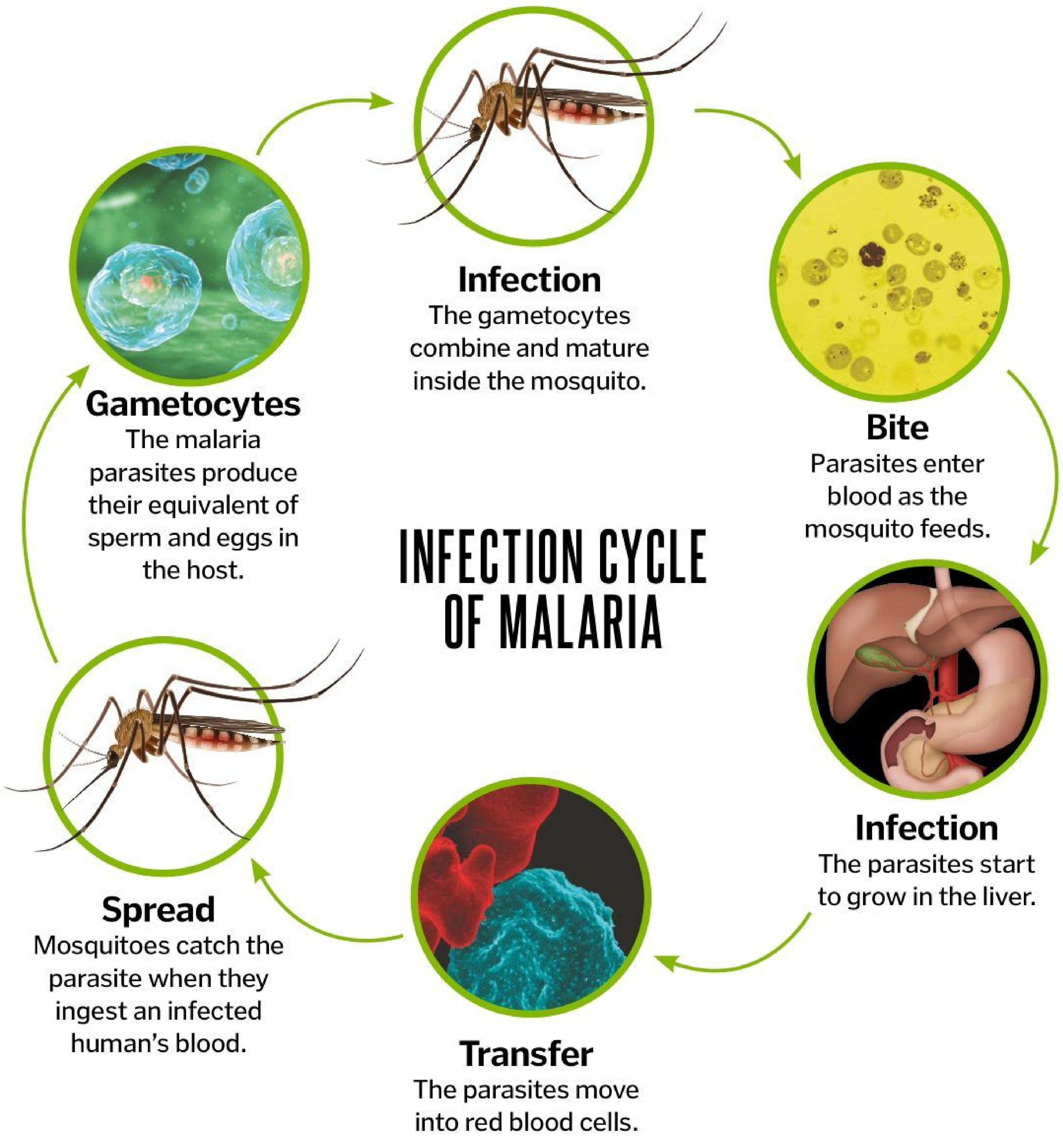
GLOBAL ELIMINATION IS TOUGH

The World Health Organization first initiated an attempt to rid the world of malaria in 1955. The idea was to use a combined attack, spraying houses to get rid of the mosquitoes and using antimalarials to kill the parasites. They had some successes in areas where the climate was moderate and mosquitoes thrive only during certain seasons, but in other places the program didn't work as well.

Mosquitoes started to become resistant to pesticides and the parasites resistant to treatments. This, combined with wars, political unrest and patchy access to resources, meant that coordinating an effective global attack against malaria became an impossible goal.

In 2015, the WHO reissued their challenge. But today we are facing even stronger versions of the parasite and vector, and new weapons are needed to eliminate them.

INFECTION CYCLE OF MALARIA



Infection
The gametocytes combine and mature inside the mosquito.

Bite
Parasites enter blood as the mosquito feeds.

Infection
The parasites start to grow in the liver.

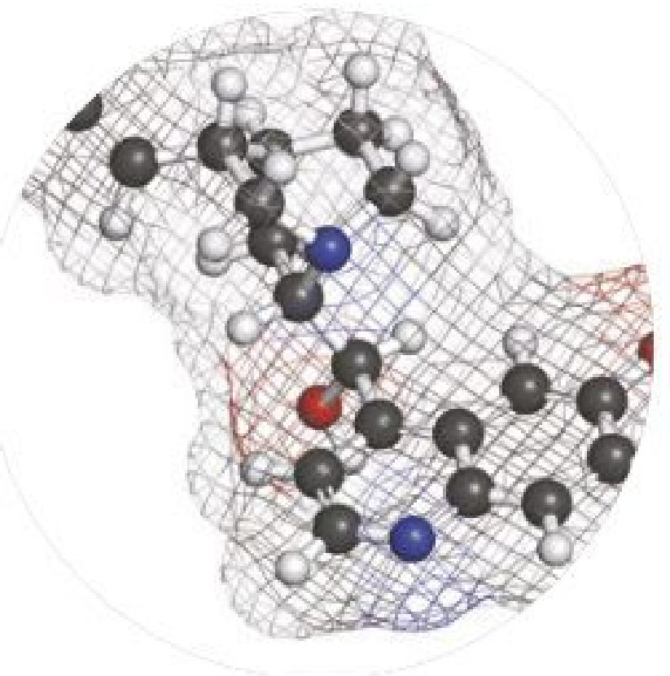
Transfer
The parasites move into red blood cells.

Spread
Mosquitoes catch the parasite when they ingest an infected human's blood.

Gametocytes
The malaria parasites produce their equivalent of sperm and eggs in the host.

TIMELINE

1600S
Peruvian tree bark is used to treat malaria, eventually leading to the modern drug quinine.



1880
The parasite that causes malaria is discovered in blood samples taken from patients.

1897
It's discovered that mosquitoes are able to transmit malaria from one person to another.

1939
The DDT pesticide is invented, allowing people to control numbers of malaria-carrying mosquitoes.

1951
Malaria is wiped out in the US after a government eradication programme sprays millions of homes.

2015
The World Health Organization endorses a new strategy to eliminate malaria for good.

FUTURE
Malaria-carrying mosquitoes are wiped out by genetically modified insect mates.

FUTURE
World declared malaria-free thanks to the eradication campaign.

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HALTING HEART ATTACKS AND STROKES

DISEASES OF THE HEART AND BLOOD VESSELS ARE THE WORLD'S BIGGEST KILLERS

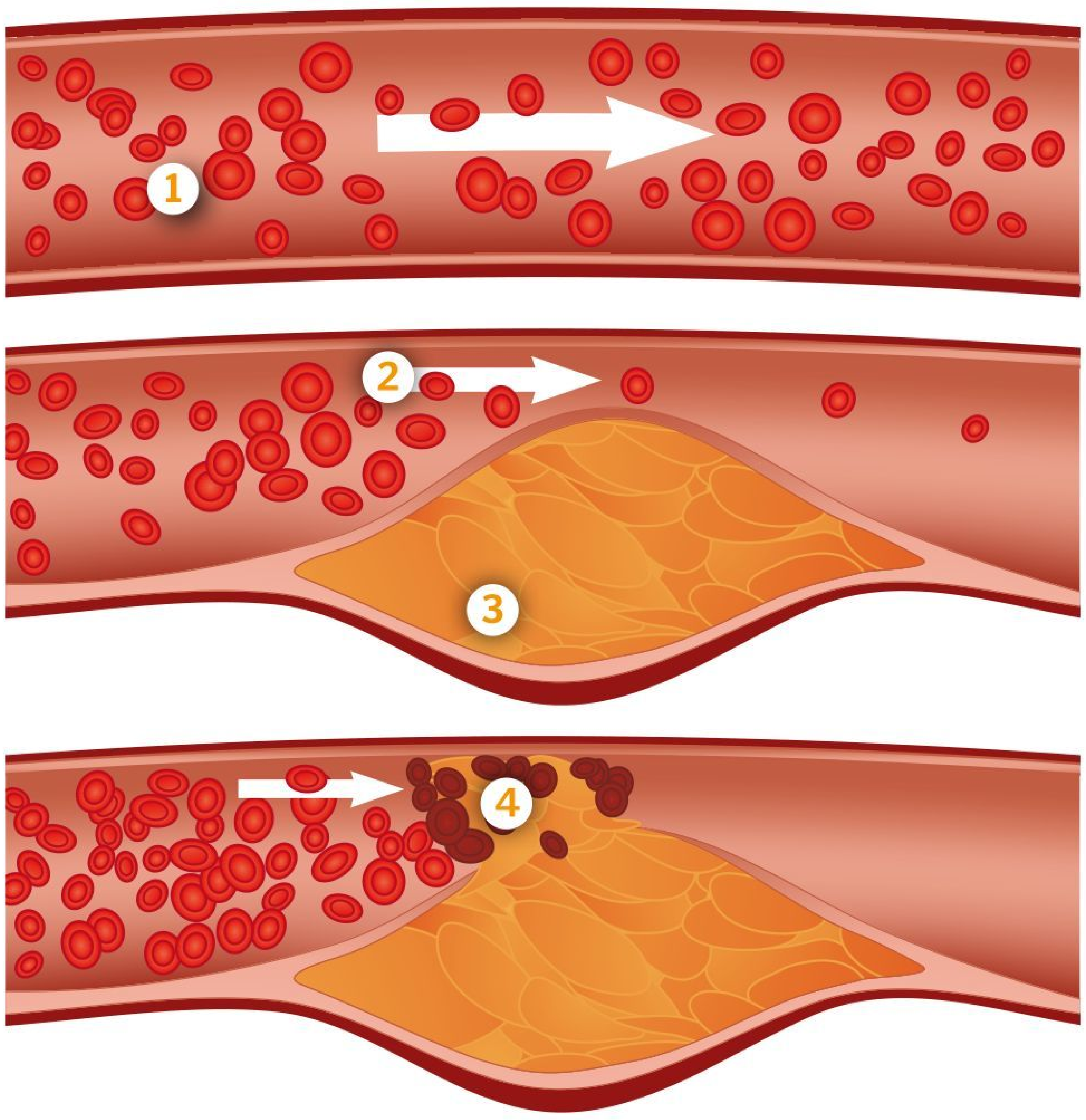
When arteries and veins become clogged with fat, rough plaques form and narrow the tubes. As the blood tries to force its way through it swirls and twists and more damage is done. The fatal blow comes when parts of the blockage break away. Clotting molecules in the blood interpret the roughness as a cut that needs to be sealed. As a result they start to build a clot, and as the circulating blob gets larger, it eventually becomes lodged in the tubes, cutting off the blood supply.

The damage can't always be repaired, but the latest research could change that for the future. Stem cells are cells that haven't yet decided which part of the body to become. With some coaxing in the lab, they can be converted into new blood cells, new skin cells, or even new heart muscle. Harvard scientists have already made a life-size beating heart by convincing stem cells to become heart muscle and growing them on a scaffold. In the future, custom organ replacements could be made artificially on demand.

If this doesn't work, another option is gene therapy, which is already being trialled for heart failure. Genes are delivered to the cells, telling them to make different molecules and potentially allowing the body to be reprogrammed from the inside out.

HOW HEART DISEASE STARTS

THE SLOW ACCUMULATION OF FAT CAN LEAD TO A DEADLY BLOOD CLOT



1 NORMAL VESSEL Healthy blood vessels have smooth internal walls, allowing the blood to slip easily around the body.

2 DISRUPTION When a blockage appears in the vessel, the blood quickly becomes backed up.

3 PLAQUE Fatty deposits in the wall of the blood vessel cause it to bulge, narrowing the tube.

4 CLOTTING A clot starts to form on the roughened surface, and the blood vessel becomes clogged.

WHY HAVEN'T WE CURED IT?

Cardiovascular disease is difficult to treat once a catastrophic event has happened; strokes and heart attacks deprive vital organs of oxygen, causing the affected tissue quickly dies. If you have a heart attack outside of a hospital, you have just a one in ten chance of surviving, and quarter of people who suffer a stroke will die within a year.

In order to meaningfully improve treatment of cardiovascular disease we need to be able to repair or replace damaged tissues, or we need to prevent it happening in the first place. Neither one is easy to do.

TIMELINE

1899
Pharmaceutical company Bayer begin manufacturing a new drug called aspirin in Germany.

1930
The defibrillator is invented, allowing stopped hearts to be restarted with electricity.

1958
The first implantable pacemaker is installed, allowing the heart to be controlled.

1960
The first heart bypass surgery is performed to divert blood around damaged vessels.

1967
The first human heart transplant is performed, allowing damaged organs to be replaced.

1987
The first cholesterol-lowering statin drug hits the market, helping to prevent heart attacks.

FUTURE
Custom-grown replacement hearts are produced from people's own stem cells.

FUTURE
Gene therapy is used to reverse the damage done by heart attacks.

Cardiovascular disease killed **17.2 million** people in 2012

Heart attack symptoms include chest, arm and jaw pain, sweating and vomiting

2s

Someone has a stroke every 2 seconds

There are over 2.5 million heart attack and stroke survivors in the UK

Men are more likely to die of heart disease than women

A third of adults in the UK have high cholesterol

The most important risk factors are smoking, diet, exercise and alcohol intake

Stroke symptoms include sudden weakness on one side of the body, confusion and slurred speech

Heart disease and stroke are the first and second most common causes of death

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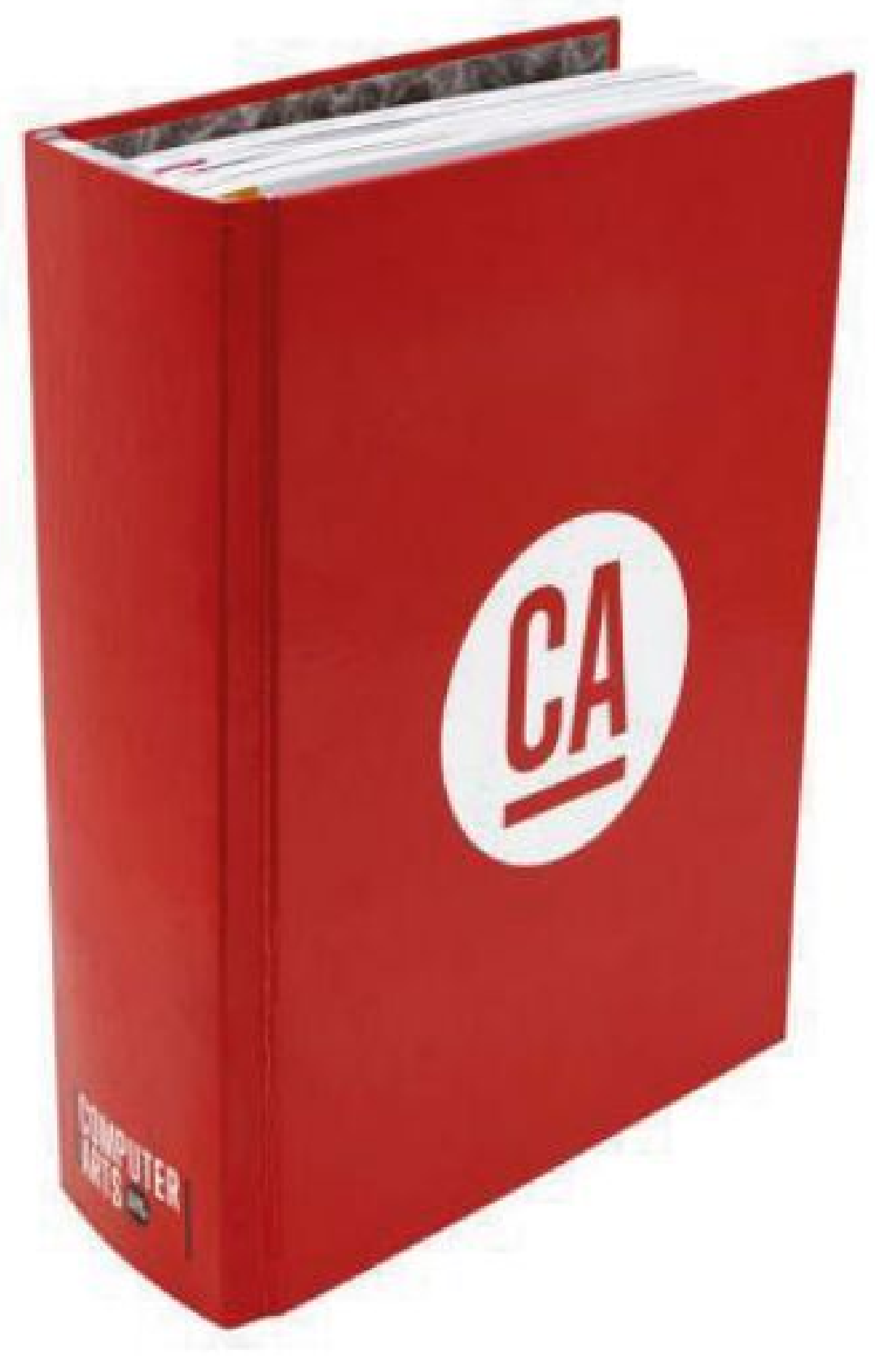

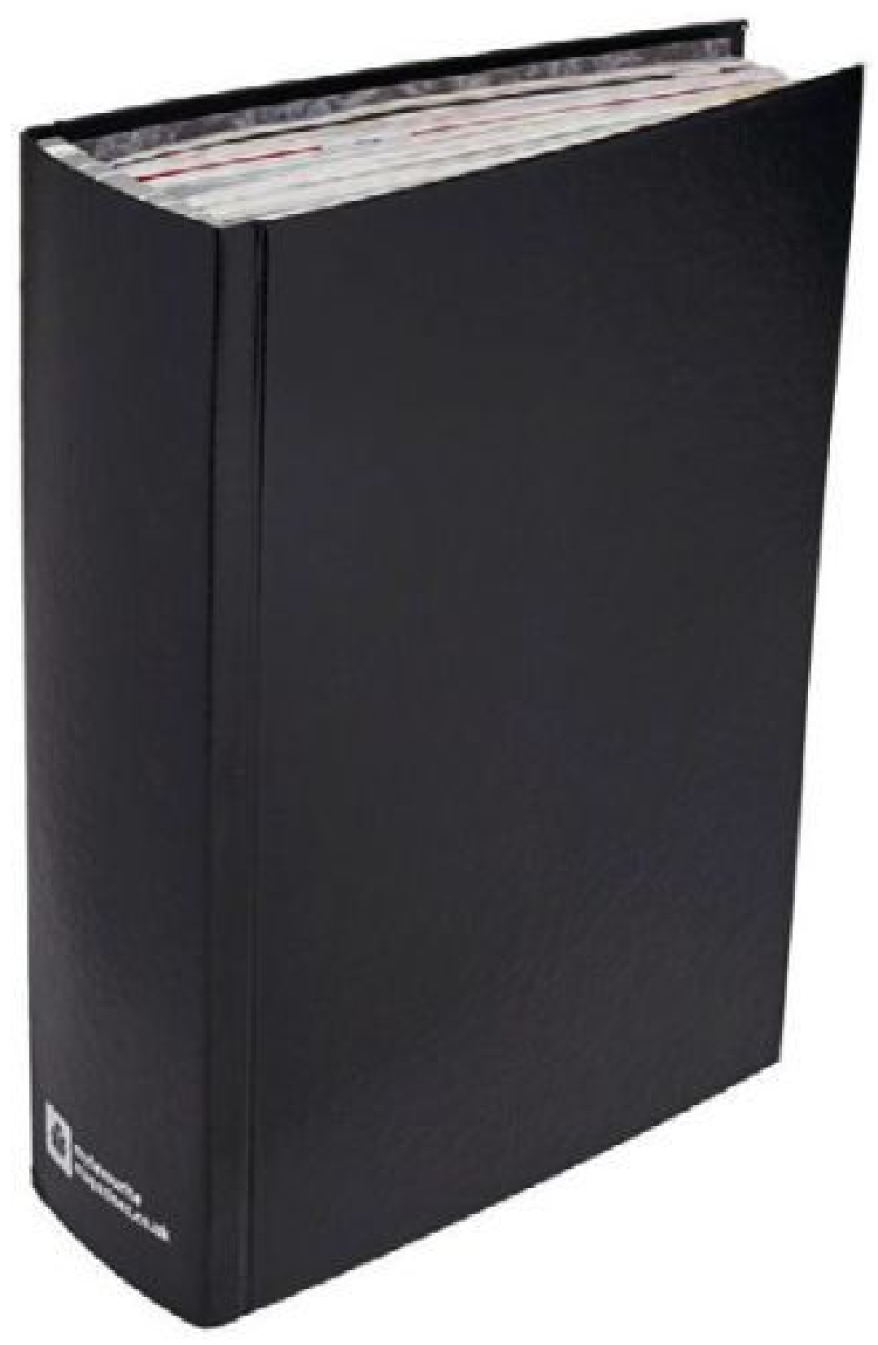

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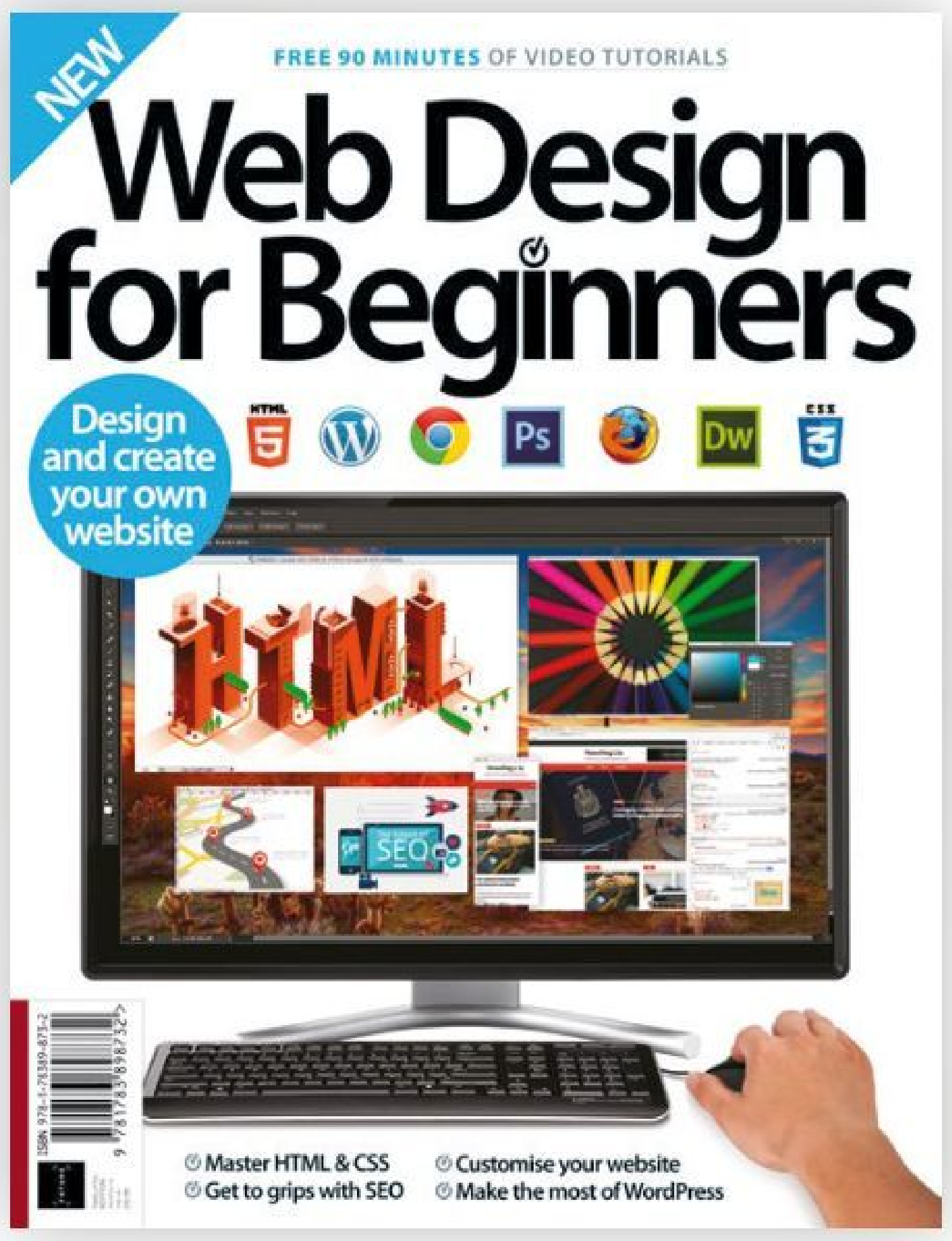
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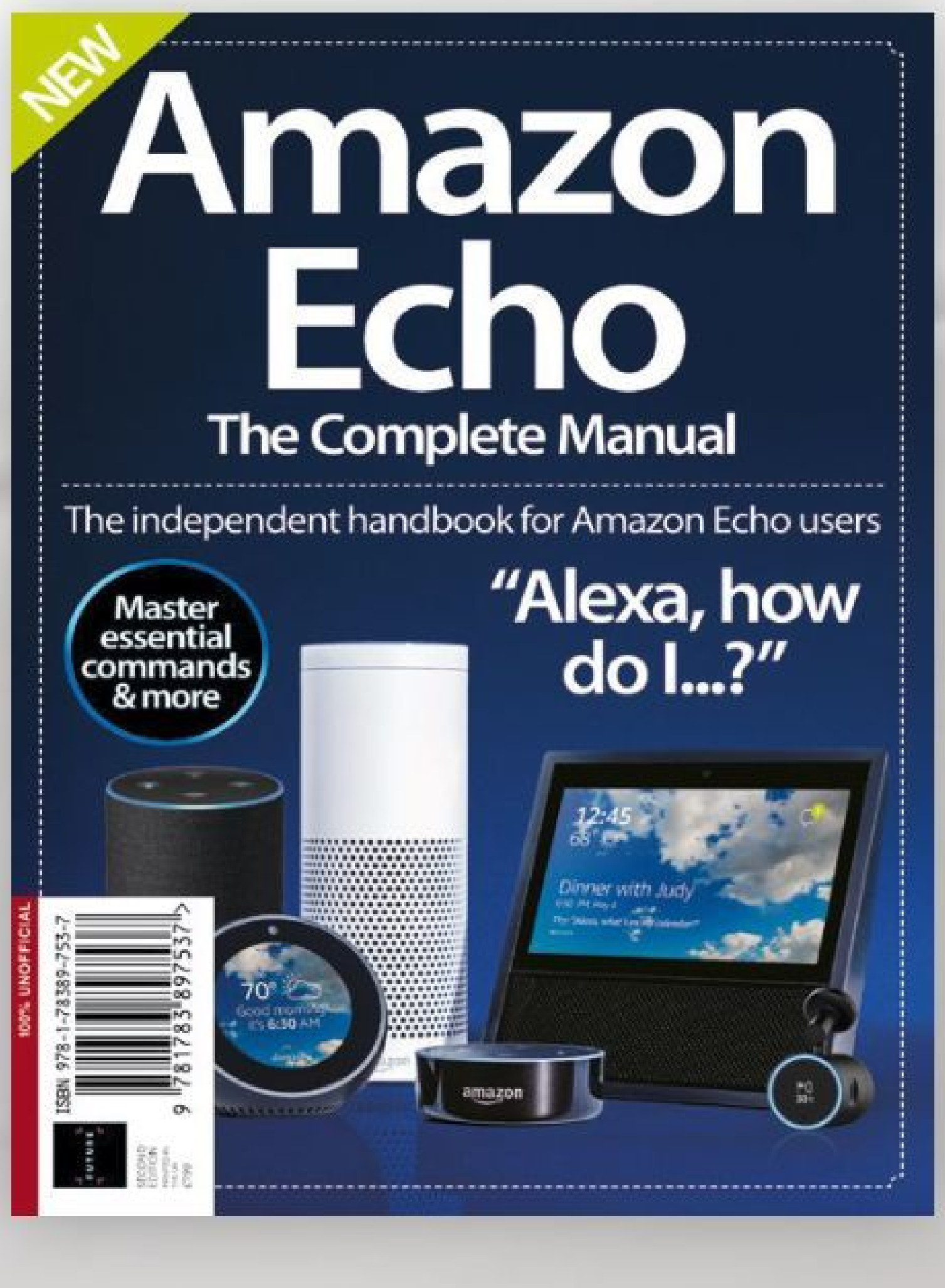
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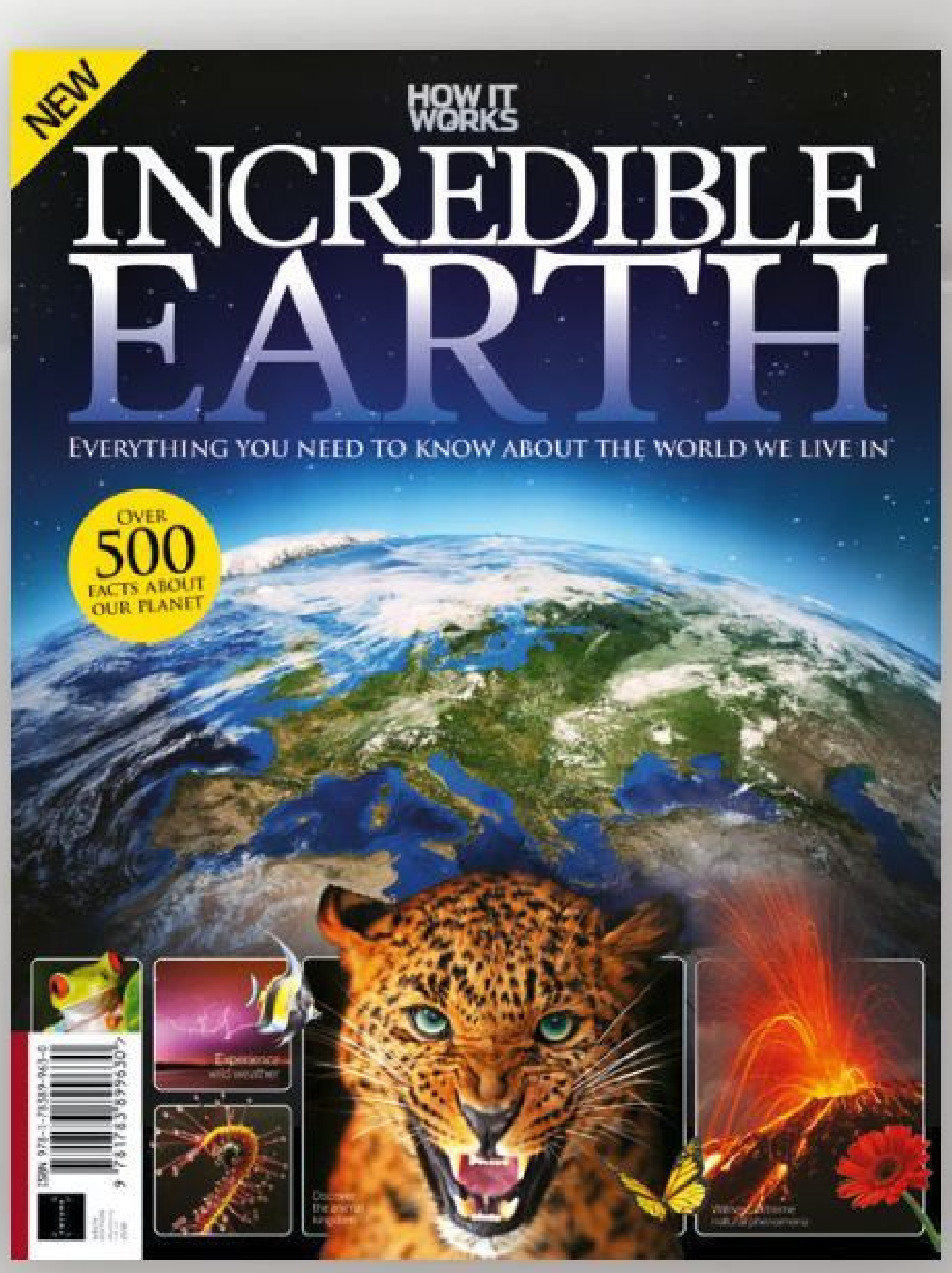
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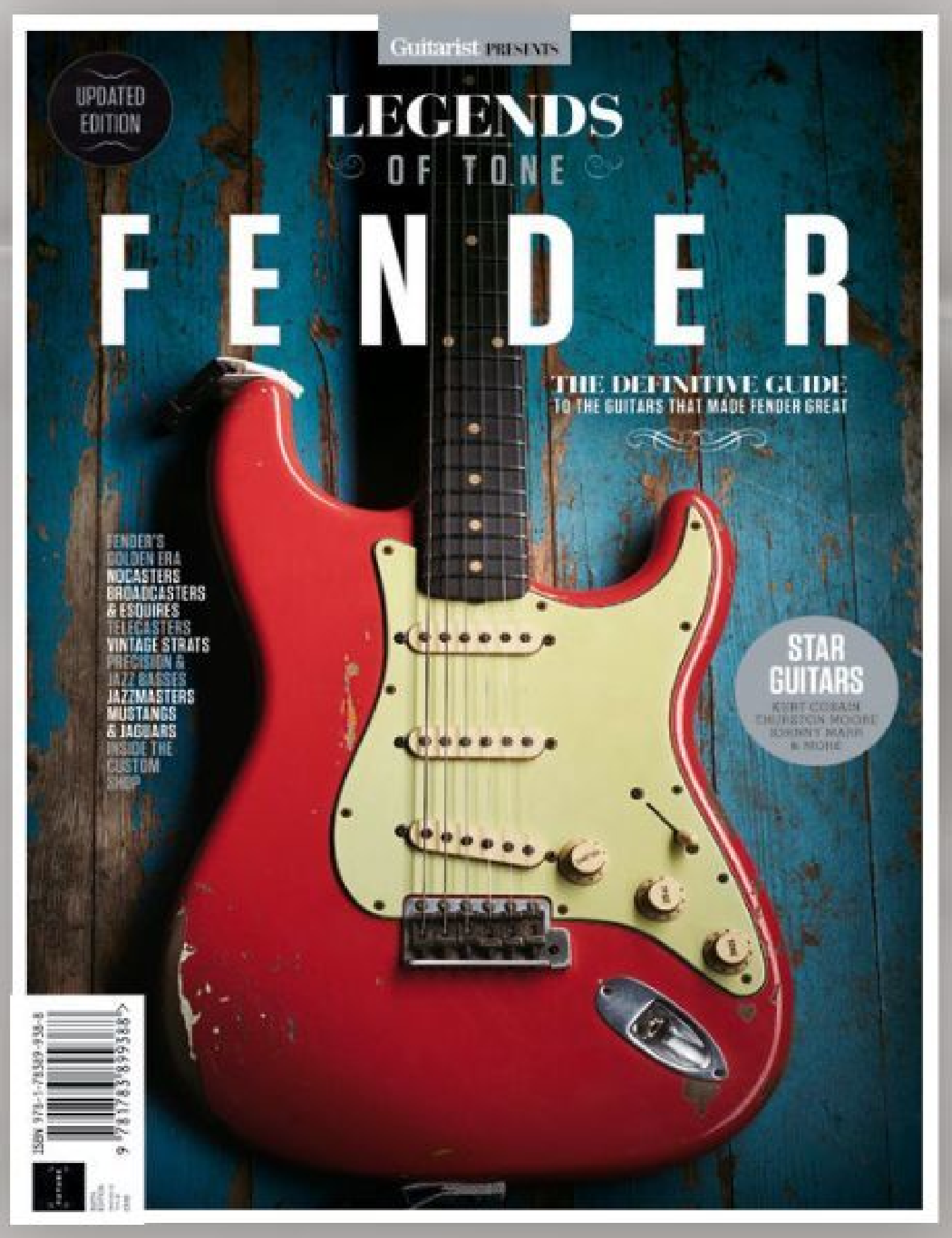
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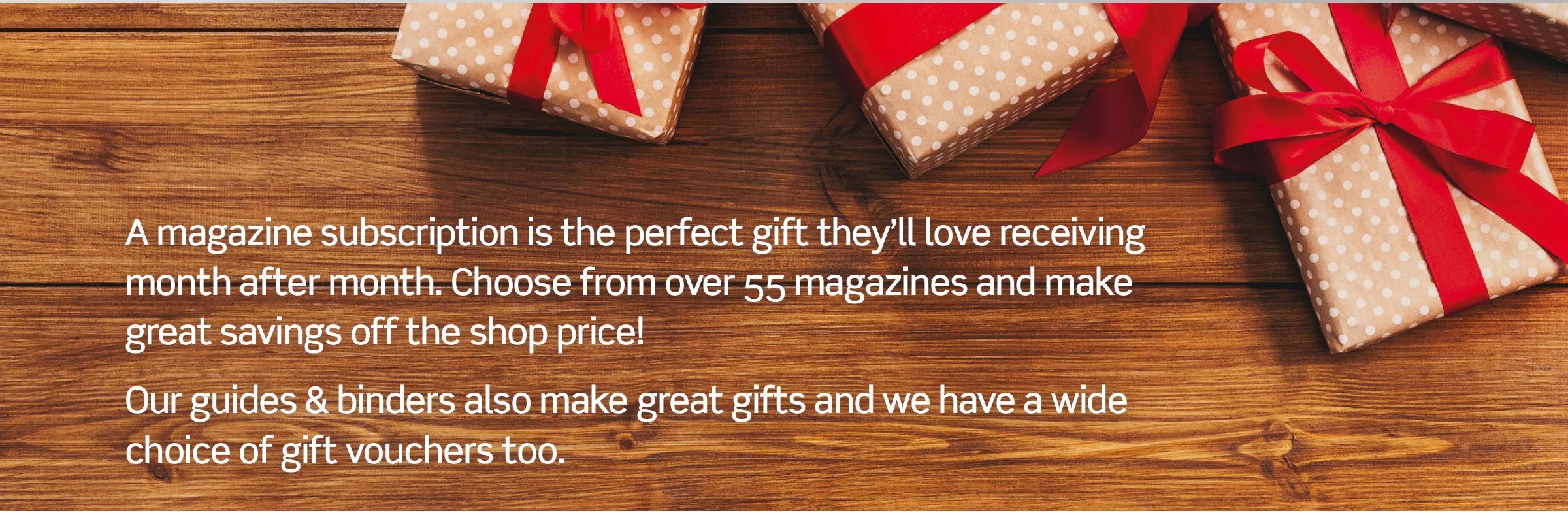

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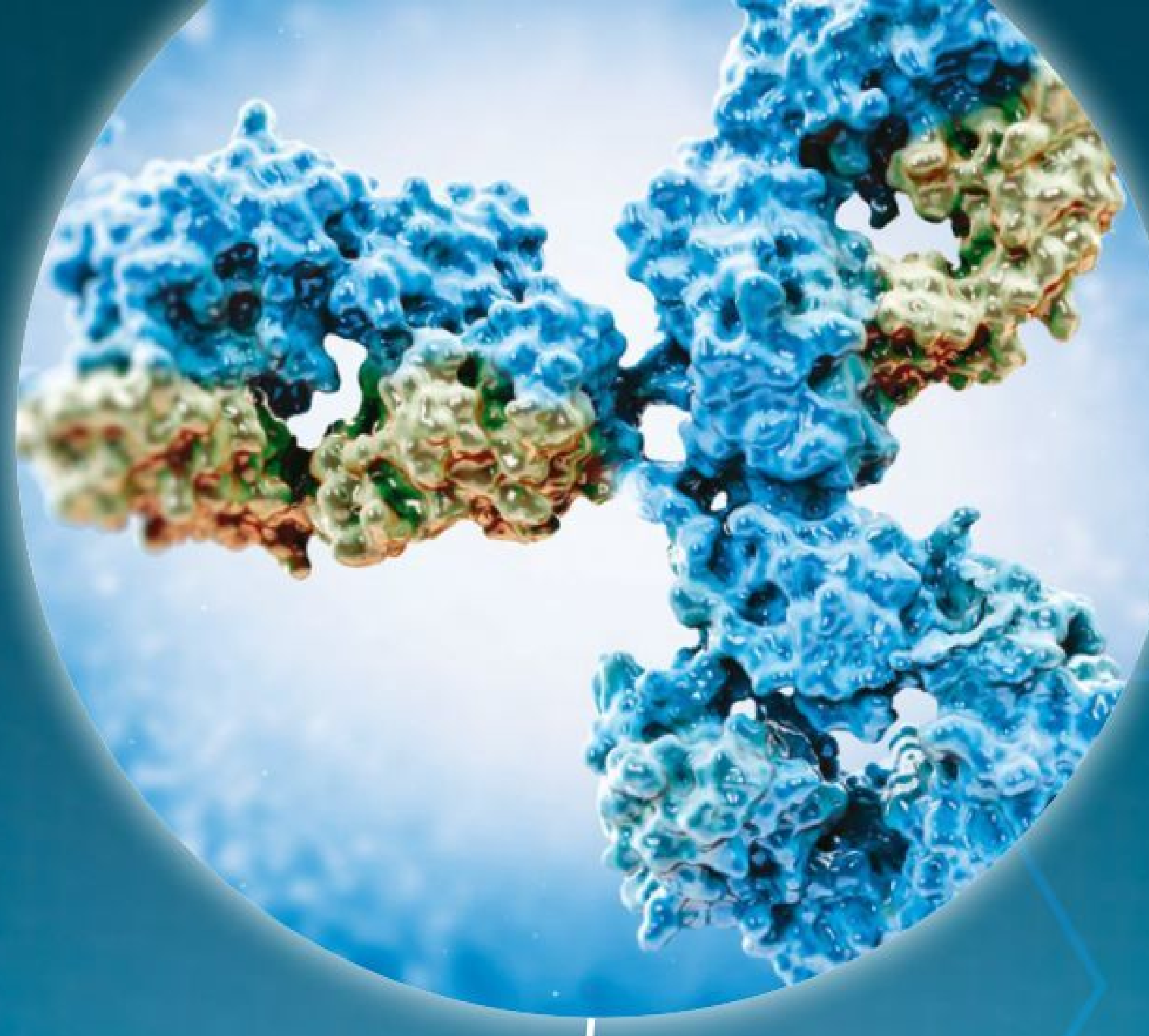

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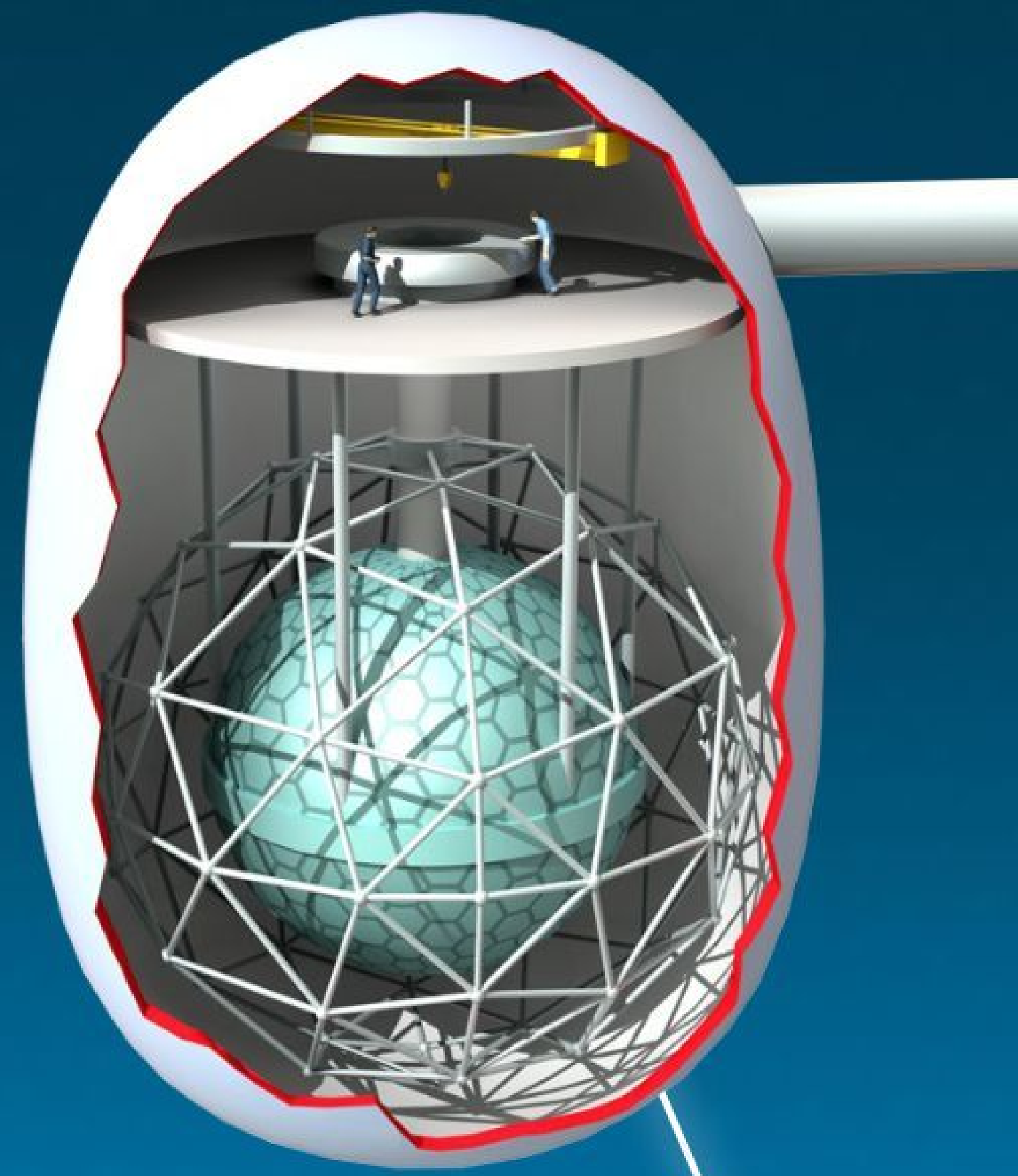

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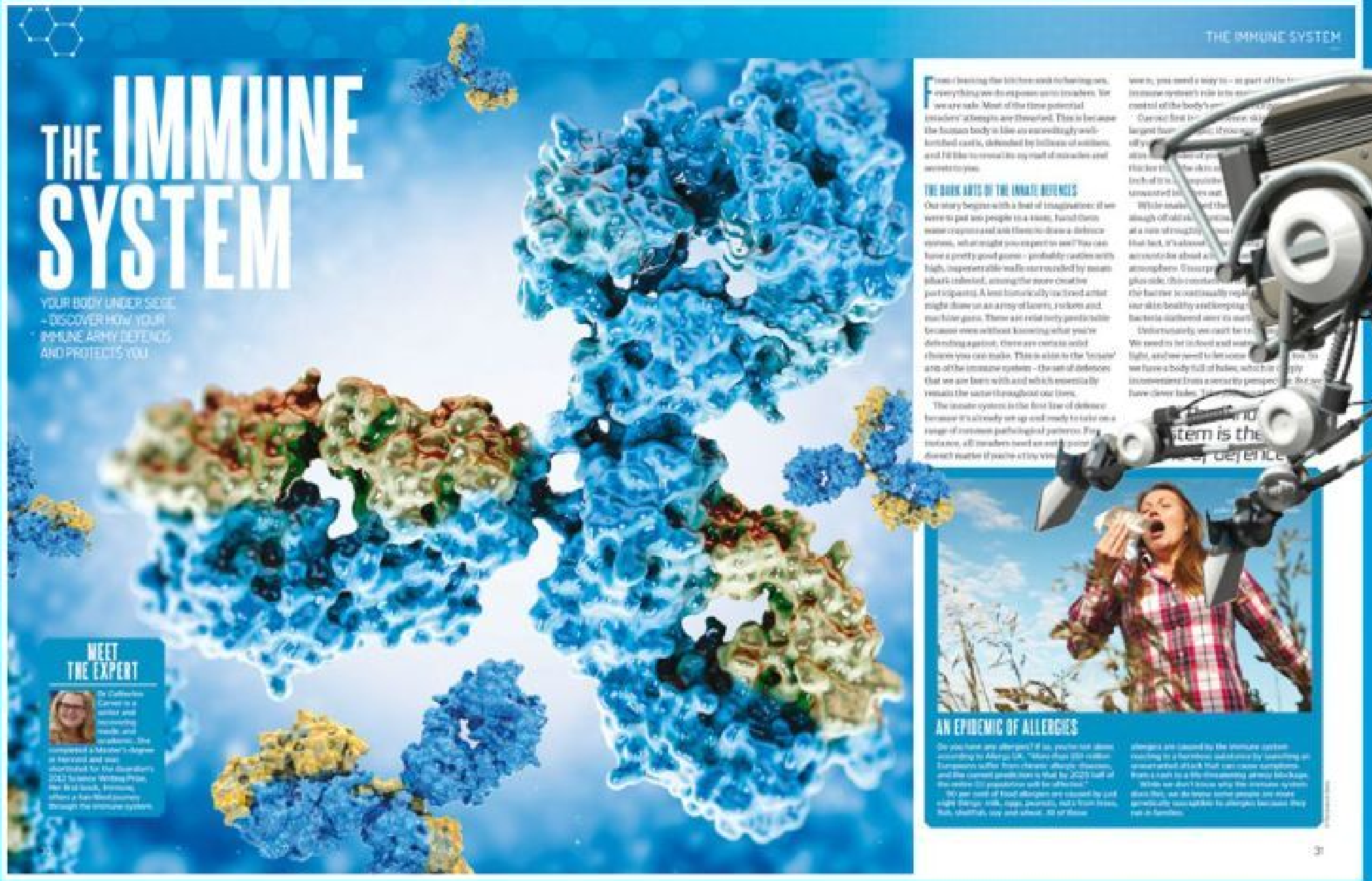

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